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ORIGINAL CONTRIBUTIONS

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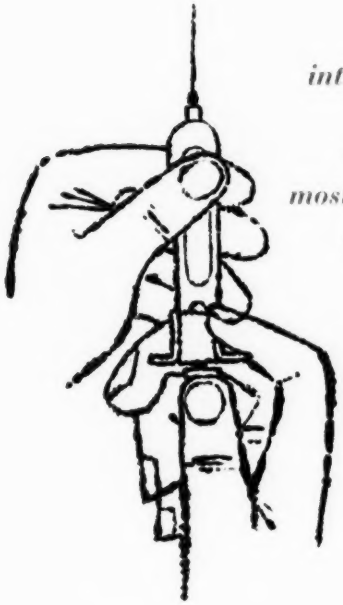

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NUTRITION AND BLOOD PRESSURE

C. M. Wilhelmj, M. D., John McDonough, M. S., and H. H. McCarthy, M. D., Omaha, Nebraska.

ELEVATED blood pressure is a symptom and like most symptoms may be a part of the clinical findings in several quite unrelated organic or functional abnormalities. Some of the conditions in which elevated blood pressure is a symptom are rare and infrequent, while others are more common. Blood pressure readings which deviate from the accepted normal ranges must be evaluated, not alone, but as part of the entire closely integrated functional unit. It is well known that diet and the nutritional level may profoundly influence blood pressure and heart rate, and because of the universality of these effective factors, their influence deserves broad and careful study. The following review shows many important and established relationships between blood pressure and nutrition but also points to many deficiencies in present day knowledge of the subject.

I The Relationship of Obesity and Body Habitus to Blood Pressure

In the light of present day knowledge, there is only one cause of obesity; namely, the intake of more energy in the form of food than is expended in the total activities of the body. The causes of the excess food intake are very numerous and complicated and probably include psychic, neurologic, endocrine and metabolic derangements of many kinds but the final result in all types is that the metabolic mill is loaded with excess energy which is mainly converted to fat which is stored in the depots. The handling of this excess food constitutes a strain on most physiological systems and metabolic functions and may cause wide spread damage to many organs (1).

Today most clinicians accept the statement that the blood pressure in obese subjects is higher than in underweight subjects, and that reduction of body weight will lower the pressure in overweight subjects. In view of the nearly universal acceptance of this concept, it is important to review some of the earlier literature upon which it is based. Hartman and Ghrist (2) studied 2042 unselected case histories taken from the files of the Mayo clinic. The patients were 15 years or more in age. The cases were divided into six groups ranging from 26 to 50 percent underweight up to 51 to 75 percent overweight. In both males and females there was an almost perfect step-like increase in systolic pressure from the most underweight to the most overweight group. In females the diastolic pressure showed a similar progressive increase but in males the diastolic pressure showed rather poor correlation with weight, a fact which the authors explain as being due to the greater difficulty in obtaining accurate diastolic pressures with the ausculatory method. Terry (3) observed that 58 percent of the admissions to an obesity clinic had hypertension and that weight reduction often resulted in spectacular falls in pressure. The diet used in reduction was a *high protein* low calorie diet. Robinson, Brucer, and Mass (4) studied 10,833 subjects. They used the "ponderal index" $\frac{\text{(weight in pounds)}}{\text{(height in inches)}}$ instead of body weight and found that as the index increased there was a progressive increase in both systolic and diastolic pressure in both males and females for all ages. Similar relationships between body weight and blood pressure were emphasized by other observers (5, 6, 7, 8). On the other hand, Huber (9) studied 1332 army personnel but his data did not show very high correlation between body weight and systolic pressure.

Larimore (10) studied 417 factory workers and used body habitus instead of body weight. It was found that the asthenic type had the lowest blood pressure and the sthenic type the highest. Modern knowledge of the psychic and physiological differences between these body types is in general in agreement with these findings. Adlersberg, Coler and Laval (11) made a specific study of the effect of weight reduction on the course of arterial hypertension in 54 patients and found that weight reduction was associated with a decrease in blood pressure in 72%. A recheck of 15 patients three years later suggested that the course of the disease was more favorable in those who maintained their weight at the reduced levels than in those who gained weight. They emphasized that overweight is only one of many contributing factors in arterial hypertension and that weight loss with a lowering of blood pressure may have no effect on the vascular changes in the fundi. Wood and Cash (12), in a beautiful experimental study on dogs, found that the systolic pressure rises with a gain in weight and falls with a loss, while the diastolic pressure shows little variation. Terry (3) also found in human subjects that the systolic pressure changed more with a gain or loss of weight than did the diastolic. Starling (13) cited observations on tuberculous patients which showed that a high caloric intake and a gain in weight caused an increase in systolic blood pressure.

All these studies show that there is a definite tendency for blood pressure to rise and fall parallel with body weight, but they leave one important question unanswered: Is body weight per se the factor which influences blood pressure or is it the type of food in which the obese subject over-indulges? The diet of obese subjects is usually high in either carbohydrate or fat or both and correspondingly low in protein.

II The Effect of Fasting and Chronic Caloric Undernutrition

(A) *Fasting.* While fasting and prolonged chronic caloric undernutrition have many features in common, there are also many definite differences (14). Depression and apathy are prominent in chronic undernutrition, while in fasting, at least in the early stages, "euphoria and states of excitement are not uncommon" (14). The excitement and sense of well being are

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Departments of Physiology and Pharmacology and Surgery, Creighton University School of Medicine, Omaha, Nebraska.

often suggested by the behavior of healthy fasting dogs (15). In contrasting the two conditions Keys (14) states, "It may be presumed that fasting is a greater, certainly a more abrupt emergency, and therefore a stronger stimulus to mobilize defense mechanisms in the body." Selye (16) considers fasting to be an effective alarming stimulus which produces pronounced counter shock phenomena within 48 to 96 hours. The counter shock phenomena are probably due to stimulation of the pituitary-adrenal system, hence, many of the characteristic features of the alarm reaction (eosinopenia, lymphopenia, thymic and lymphoid tissue atrophy, gastrointestinal ulcers and hemorrhage) may be present. In prolonged chronic undernutrition this rapid mobilization of the defense mechanisms of the body is not so evident. These differences between acute starvation and chronic undernutrition are reflected in the differences in the behavior of the blood pressure and pulse rate in the two conditions. When a healthy well nourished dog is suddenly deprived of food (water allowed ad libitum), the early cardiovascular reaction is usually an initial, abrupt fall in both systolic and diastolic blood pressure and pulse rate. However, this is often quickly followed by an abrupt elevation of blood pressure and pulse rate, frequently to values definitely higher than the control levels. Following this, the daily blood pressure begins a series of irregular saw tooth elevations and depressions which gradually become lower and lower until finally the blood pressure reaches a low stable level with few fluctuations. The pulse rate may show similar behavior. The early fluctuations of blood pressure and pulse rate are often very extreme. The degree and duration of this early fluctuating blood pressure are directly proportional to the nutritional level of the animal before the beginning of starvation. It may be very pronounced and last as long as 65 days (with gradual diminution) in a dog on a prefasting luxus consumption diet or it may be very slight and last only from one to seven days in a dog previously maintained on a low maintenance level of nutrition. The stable fasting level which is finally reached is independent of the previous level of nutrition and is surprisingly constant in repeated fasts on the same dog (15). The stage of fluctuating blood pressure and pulse rate is obviously the counter shock stage referred to by Selye (16). The low stable fasting level finally reached probably represents a stage of depletion in which the factors causing the counter shock phenomenon are exhausted or no longer effective.

Very few studies appear to have been made on the human subject during prolonged total fasting in which blood pressure and pulse rate were observed daily. In the classical study made by Benedict (17) on "Subject L" during a 31 day fast, frequent determinations of blood pressure and pulse rate were made and the results appear to be similar to those observed by Wilhelmj et al (15) on fasting dogs. During World War II some sketchy and incomplete observations made on persons suddenly subjected to total fasting suggested similar behavior of the blood pressure and pulse rate (18).

(B) *Chronic Undernutrition.* The effects of experimentally produced chronic undernutrition on the blood pressure and pulse rate of human subjects have been reported in the classical studies of Benedict and Roth (19), Benedict, Miles, Roth and Smith (20) and Brozek, Chapman and Keys (21). In the studies of Benedict et al (19, 20) the subjects were first placed on a restricted diet until a weight loss of 10 to 12 percent occurred; they were then placed on a low maintenance diet to maintain this weight. The pulse rates dropped to low levels (ranges of 20, 30, 40 beats / minute). The fall in blood pressure was very prompt and profound. After one week on the low maintenance diet, the blood pressure of eleven men dropped from a mean of 120/83 to a mean of 102/69. Diastolic pressures of 60 or below were common. The blood pressure of three subjects is of special interest. On a normal diet they were 142/90; 130/90 and 120/90. The pressure of the first subject was considered to be hypertensive for a man of his age. On the 8th day of the low maintenance diet the pressures were 120/78; 106/70 and 105/80 respectively. On the 14th day the pressures were 100/65; 95/65 and 105/80 and on the 22nd day they were 100/65; 100/70 and 90/70 respectively. Thus, it is seen that the drop was profound and prompt with no evidence of the counter shock phase which is seen when sudden fasting is imposed on a previously well nourished animal. The same prompt fall in blood pressure and pulse rate, without counter shock phenomenon, was observed by Wilhelmj, Waldmann and McGuire (15) when dogs, previously given a low maintenance diet, were subjected to fasting.

When human subjects were placed on a low maintenance diet Brozek, Chapman and Keys (21) observed a reduction in body weight of 23.9 percent in 6 months. The mean systolic pressure for the group fell from 106.5 to 94.7 (a decrease of 11 percent), while the diastolic fell from 69.9 to 64.5 (a decrease of 7.7 percent). The mean pulse rate for the group reached a value of 37 beats/minute. There was a striking decrease in the size of the heart. The basal metabolic rate declined to 39.9 percent. It is obvious that on the low maintenance diets the work of the heart was drastically reduced. One of their subjects developed evidence of cardiac decompensation during realimentation on a large and unrestricted diet, but this was controlled by simple dietary restriction.

In the same report Brozek, Chapman and Keys (21), give a detailed description of the cardiovascular changes noted during and after the siege of Leningrad. In brief, during the period of drastic food restriction the number of hospitalizations for cardiovascular conditions decreased markedly, but promptly increased when the siege was lifted and the food supply became abundant. Similar observations have been reported from other countries during and after World War II.

Hultgren (22) has presented a detailed account of the clinical and laboratory observations in starvation as observed during World War II. Out of 29 cases reported, the blood pressure in 12 cases (41 percent) ranged from a low value of 75/45 to a high value of 98/65. These blood pressure levels on starving human subjects are within the same ranges as those reported by Wilhelmj, Waldmann and McGuire (15) for the stable fasting values in dogs.

Taylor and Keys (23) in a study of adaptation to caloric restriction have shown the striking decrease in

the energy cost of doing work and the parallel decrease in the work of the heart which occur as a result of restriction of food intake and consequently, decrease in body weight.

These studies show clearly that a reduction in food intake and a reduction in body weight result in pronounced decreases in blood pressure, pulse rate and the work of the heart. It appears shockingly evident that overnourished Americans are literally eating themselves to death and that the medical profession is not making full use of a simple but highly effective measure for treating hypertension and cardiovascular disease; namely, a reduction of food intake to the maintenance level.

III PROTEIN CONSUMPTION AND BLOOD PRESSURE

This is one of the most controversial and confused phases of the subject under discussion. Much of the clinical literature is based on impressions often highly colored by emotional thinking. Clear cut experimental evidence is not abundant. Further, confusion is actually added by animal experiments, possibly because of species differences and differences between normal and experimentally pathological animals.

The auto-intoxication theory of Metchnikoff, the identification of indol and skatol in the intestine as products arising from the putrefaction of protein, the claims of Chittenden on the virtues of a minimal protein diet, certain animal experimental studies interpreted as demonstrating the detrimental effects of high protein diets on longevity, and evidence suggesting kidney damage by protein were all important factors in shaping the concept that protein is a cause of hypertension and should be eliminated or drastically reduced in treatment.

(A) *Studies on Human Subjects*

The paper of Reisman (24) and the discussion by L. F. Bishop are characteristic of medical thought on this subject in the first quarter of the 20th century in that both advocate a low protein diet in the treatment of hypertension. Hamman (25) in a fairly complete review of the knowledge of hypertension in 1917 states, regarding protein: "I can only say that a general impression of its harmfulness is firmly established and in accordance with this view it is customary to devise a diet low in protein with meat completely eliminated or nearly so."

Mosenthal (26) was one of the early clinical investigators who denied that a high protein diet raised blood pressure or that a low protein diet lowered it. He referred to the classical studies of Benedict and stated that one of the most important factors in therapy was a low caloric mixed diet to reduce body weight. Later (27) he presented a clinical study on a patient with hypertension. The total caloric intake was kept constant at 2065 calories while the protein content was progressively lowered from 125 grams to 50 grams daily over a period of 39 days without a change in the level of the blood pressure. He again stressed the fact that a high caloric intake and obesity were more important in raising the blood pressure level than is a high protein diet. He found fat and carbohydrate had specific effects on blood pressure only in so far as they caused obesity. In a later paper Ashe and Mosenthal (28) stated that "there is no evidence to show that a low protein diet followed by a hypertension subject will materially reduce the blood pressure, provided there is no anemia." A dietary survey of 1000 residents of New York showed that people with hypertension do not habitually eat more protein than normotensives.

In 1921 Squier and Newburgh (29) published their frequently quoted paper showing that very high protein diets will cause red blood cells and albumen to appear in previously negative urine of patients with essential hypertension or normal subjects. In this paper they state that the blood pressure was not elevated by the high protein intake. In a later paper Newburgh, Falcon-Lesses, and Johnston (30) reported that when a human subject whose urine contained no albumen and "less than the average number of casts" lived for six months on a diet in which one-third of the calories were contained in beef protein, a significant albuminuria and a twenty fold increase in casts occurred. However, they state that the basal blood pressure before starting the diet was 110/80 and was uninfluenced by the diet. McLaughlin and Shay (31) working in our laboratory on human subjects have confirmed the findings of Squier and Newburgh (29) that a high meat diet will cause the appearance of red blood cells (microscopically) in previously negative urine without a change in blood pressure. This finding has been confirmed by others on rats (32) but the prognostic significance of the fact is not clear. Strouse and Kelman (33) found no evidence of renal damage by feeding 150 grams of protein daily. They also emphasized that they found no relationship between the protein intake and the blood pressure level in cases with hypertension and hypertension and nephritis. Keys et al (34) found that the protein content of the recovery diet following prolonged severe inanition was without consistent effect on the systolic or diastolic blood pressure or pulse rate.

Levine (35) determined the blood pressure of 823 Eskimos ranging from 8 to 80 years of age who were living on their natural high protein diet. In the age group 21-80 years, the blood pressure of the males averaged 109.9/71 and of the females 109.6/70.6. Systolic pressures of 90 were often encountered with no loss in vigor or strength.

One of the most conclusive experiments on human subjects was that made on the Arctic explorers Stefansson and Anderson (36). They lived on an exclusive meat diet for one year. Stefansson maintained a blood pressure of 105/70 during the entire experiment while Anderson's pressure was 140/80 at the beginning and 120/80 at the conclusion of the experiment. No albumen, casts or blood were found in the urine of either subject at any time during the experiment. P.S.P. excretion and urea clearance tests were also normal.

(B) *Studies on Animals*

Page and Lewis (37) studied dogs with experimental renal hypertension and found that there was no significant change in blood pressure with diets high either in protein or in carbohydrate. Guerrant, Scott and Wood (38) found that the administration of a high protein diet (lean raw meat) to normal dogs or

dogs with experimental renal hypertension for either long or short periods of time failed to produce a consistent rise or fall in systolic or diastolic blood pressure. Allen and Cope (39) studied dogs with explanted kidneys so that the effect of diet on kidney size could be determined. They found that high protein diets caused no increase in blood pressure; in fact, they tended to lower it. Alpert and Thomas (40) studied the effect of dietary protein on the blood pressure of normal dogs and dogs with various types of hypertension and found that high or low protein diets had no consistent effect on blood pressure. Philipsborn, Katz and Rodbard (41) studied the effect of high protein diets on dogs with experimental renal hypertension. They classified the dogs into groups depending upon the degree of hypertension and renal insufficiency. In only two animals, both with moderate renal failure, was a significant rise in blood pressure elicited by a high protein diet. Machlachlan and Taylor (42) produced hypertension in dogs by removing one kidney and placing the other in a cast to prevent any increase in size. In one such dog the blood pressure rose from 151 to 176 when the diet was changed from dog biscuits to 800 grams of lean meat daily. When again placed on the low protein diet of dog biscuits, the blood pressure promptly fell and reached the previous level in one week. This was repeated several times. They state that the change in blood pressure occurred so fast that it was not due to change in weight. Increasing the work of the kidney by feeding 50 grams of urea daily had a hypertensive effect of the same magnitude as that of the high meat diet.

Wilhelmj, McGuire and Waldmann (43) found that when healthy dogs were realimented with high caloric diets following prolonged fasting, there was less evidence of cardiovascular stress with diets high in protein (horse meat) than with isocaloric diets high in carbohydrate.

In the experiments on dogs reviewed above, most of the findings fail to support the thesis that protein will elevate the blood pressure of normal or experimentally hypertensive dogs. Philipsborn et al (41) found only two and Machachlan and Taylor (42) only one animal which showed elevation of blood pressure on high protein diets.

Handler and Bernheim (44, 45, 46, 47) have studied rats with experimental renal hypertension and have found that the level of the blood pressure is directly proportional to the level of protein intake. Their evidence indicates that ACTH production is the responsible factor and that the production of ACTH varies directly with the protein content of the diet. ACTH did not raise the blood pressure of normal rats regardless of diet (47). In rats made hypertensive by choline deficiency at weaning age, the same relationship between the protein content of the diet and the level of the blood pressure was demonstrated (48).

Constantinides (49), using rats, showed that the alarm reaction to short stresses was more intense on a diet high in amino acids than on a diet high in carbohydrate. Here also ACTH production may be the responsible factor.

The findings of Handler and Bernheim show that in rats with experimental renal hypertension the relationship between the blood pressure level and protein intake appears to be different from that of the dog and the human subject.

IV Sodium Intake and Blood Pressure

Space will not permit a detailed analysis of the effect of sodium intake on blood pressure, but the following salient points are important:

The studies of Handler and Bernheim referred to above and the findings of Grollman and Harrison (50) show that increasing or decreasing the sodium intake in rats with experimental renal hypertension causes parallel changes in blood pressure. Saperstein et al (51) have shown that 2 percent sodium chloride as the sole source of drinking water will raise the blood pressure of normal rats. Lenel et al (52) showed that sodium chloride ingestion caused an elevation of blood pressure proportional to salt intake in normal chickens. Wilhelmj, Waldmann and McGuire (53) and Allen (54) were unable to cause physiologically significant elevations of blood pressure by high sodium chloride ingestion in normal dogs. Even two percent sodium chloride as the sole source of drinking water was ineffective (53). This is probably due to the fact that the kidneys of normal dogs have a phenomenal ability to eliminate sodium chloride as shown by Ladd and Raisz (55). Page and Lewis (37) found that high or low salt diets failed to change the blood pressure of dogs with experimental renal hypertension. Frieden et al (56) showed that low sodium diets had no effect on the blood pressure of renal hypertensive dogs but that severe chronic sodium depletion with hyponatremia reduced the blood pressure to normal levels.

The effect of sodium restriction in human hypertensives seems to lower the pressure in some cases but not in others. Davies and Clark (57) studied a group constituting about 20 percent of essential hypertensives in which the elevated blood pressure was believed to be due to overactivity of the adrenal cortex since there were some findings suggestive of Cushing's syndrome (pseudo-Cushing's syndrome). This group showed evidence of sodium retention as indicated by a low sodium content of sweat. Other essential hypertensives showed normal sodium content of sweat. It is quite possible that the type of hypertensive studied by Davies and Clark are those who show lowering of blood pressure on sodium restriction, while other types do not.

V Effect of Carbohydrate and Fat on Blood Pressure

The general impression gained from the literature is that carbohydrate and fat have a specific effect on the level of the blood pressure only in so far as they are factors in the production of obesity. However, Selye (58) states that a diet rich in fats when fed to rats causes a pronounced adrenal enlargement. Holman (59, 60, 61, 62) has been able to produce necrotizing arteritis in dogs with mild renal lesions when fed high fat diets. He finds (62) that some dogs have shown irregular elevations of blood pressure, but that hypertension is not necessary for the production of the lesions. Vitamin E and cholesterol prevent or retard the development of the lesions.

Nelson (63) has recently reported on a group of arteriosclerotic patients with mild or moderate hypertension who were placed on a high protein low fat-cholesterol diet plus choline and inositol and B vitamins with a high pyridoxine content. These subjects initially had high blood cholesterol and a low cholesterol-phospholipid ratio. A marked hypotensive effect was observed in 76 percent of the patients with arteriosclerosis and hypertension. This seemed to be associated with a lowering of the blood cholesterol and elevation of the cholesterol-phospholipid ratio. This regimen had no hypotensive effect on younger patients with essential hypertension and normal blood chemistry. This promising finding must be verified by further work before its significance can be evaluated.

While the rice diet of Kempner is a high carbohydrate diet, its effects are usually stated to be due to its low content of sodium and protein. There can be no doubt but what some hypertensive patients are greatly improved by this diet (64). Dick and Schwartz (65) produced nephrosclerosis and hypertension in dogs and found a marked lowering of blood pressure after eight weeks on the rice and fruit juice diet. They state that the dogs often refused the diet and that all lost weight, the average loss being 19.7 percent. The authors state that no correlation could be found between the weight loss and the fall in blood pressure. A weight loss of this magnitude however, must be seriously considered as a factor of importance in the lowering of the blood pressure. Human subjects on the rice diet find it monotonous and finally unpleasant and many restrict their caloric intake and lose weight and this factor may be the chief merit of the diet.

SUMMARY

1. In human subjects and experimental animals, it has been conclusively shown that an increase in body weight elevates blood pressure, while a decrease lowers blood pressure. In human subjects, it has not been proven whether body weight per se or the dietary constitutents naturally chosen by obese subjects (high carbohydrate and/or fat and low protein) is the direct causative factor influencing the blood pressure.

2. In normotensive and hypertensive human subjects and dogs, most of the evidence indicates that high protein diets do not elevate or low protein diets decrease the level of the blood pressure. In normotensive and hypertensive rats, the blood pressure level varies directly with the level of protein intake and the evidence suggests that the synthesis of ACTH may be the link between the level of protein intake and the blood pressure in this species.

3. The available evidence indicates that carbohydrate and fat influence blood pressure only in so far as they influence body weight. High fat diets combined with minimal kidney lesions produce a necrotizing arteritis in dogs, but elevation of blood pressure is not a constant finding.

4. High sodium chloride ingestion combined with an otherwise normal diet does not cause significant elevation of the blood pressure of normal dogs, but does elevate the blood pressure of normotensive or hypertensive rats.

In some human hypertensives, restriction of sodium intake causes marked lowering of blood pressure, while others are not affected. It seems likely that those hypertensives who show a lowering of pressure with salt restriction, belong to a group where overactivity of the adrenal cortex is the causative factor.

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INCIDENCE OF ASYMPTOMATIC HIATUS HERNIA

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MOST OF the data reported in the past on hiatus hernia is from roentgenologic examinations which have been done because the patient had some gastrointestinal complaints. There are few studies in which patients without gastrointestinal symptoms are examined primarily for a hiatus hernia. The need for such a study has been previously indicated (1).

Since hiatus hernia is diagnosed more frequently today, due to a greater awareness and the use of positional maneuvers of the patient during the roentgenologic examination of the esophagus and stomach, the problem of asymptomatic hiatus hernia is of greater significance. Hurst (2), quoting Knothe, reported an incidence of hiatus hernia, in routine examinations, of 8 per cent. Schnepp (3) in a review of the literature reported an incidence for hiatus hernia of 0.2 to 8 per cent in routine roentgenologic studies. In a recent study (1) of 3448 patients, hiatus hernia was found in 8.93 per cent of routine examinations.

The literature reveals great differences of opinion as to the importance and incidence of asymptomatic hiatus hernia with little objective data. Ritvo (4) found 14 symptomless patients in a series of 60 hernias. However, Wilkinson (5) found only 4 symptomless patients in 70 cases. Moersch (6) found 19 symptomless in 246 cases. Jones (7) believed there would be no symptoms in some cases since a large number were demonstrated accidentally. Ohler and Ritvo (8) reported 9 symptomless in 136 cases of hiatus hernia. Shanks (9) thought that about 20 per cent of cases, usually in the early stages, are symptomless.

Symptomless persons have been examined for gastric neoplasms and hiatus hernia was mentioned as an incidental finding. St. John, Swenson and Harvey (10) examined 2413 persons over 50 years of age by fluoroscopy, usually in an upright position, and found 25 cases of hiatus hernia. Rigler (11) examined 544 patients over the age of 50 and noted an "appreciable number" of hiatus hernias. Sherman (12) found that "there were cases of hiatus hernia of various types and degrees."

For this study 200 ambulatory patients over the age of 50 with no gastrointestinal symptoms were selected. There were 115 females and 85 males.

Patients were examined in the morning after an evening fast. Each patient drank 6 ounces of an aqueous barium sulfate mixture. Examination consisted of fluoroscopy in the upright, Trendelenburg and prone positions. Roentgenograms were taken in the 10 degree Trendelenburg and prone positions.

Three cases of hiatus hernia were found, two in females and one in a male, an incidence of 1.5 per cent. This is comparable to the incidence of 1 per cent in St. John, Swenson and Harvey's cases (10) and the incidence of 1.3 per cent in Brick's (13) cases.

The technique used in this study should reveal most hiatus hernias and the patients were in the age group with the highest incidence of hiatus hernias. However, the incidence of hiatus hernia in asymptomatic patients is low, 1.5 per cent in this series. This differs markedly with the incidence of 8.93 per cent as found in patients with various gastrointestinal symptoms (1). One should not discard the diagnosis of hiatus hernia in patients with gastrointestinal symptoms without proper appraisal, since the incidence of hiatus hernia is much higher in this symptomatic group.

Two hundred patients with no gastrointestinal symptoms and over the age of 50 were examined by fluoroscopy and roentgenograms for hiatus hernia. Three patients, or 1.5 per cent, had a hiatus hernia. Since patients with gastrointestinal symptoms have a much higher incidence of hiatus hernia, possibly this lesion may explain the symptoms and should not be dismissed as only an incidental finding.

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SIGNIFICANT FACTS CONCERNING THE PAPILLA OF VATER

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THE DISTAL end of the common bile duct is a "blind area." Not only is observation precluded in the intact individual, but even surgical access frequently is ineffectual. Consequently, information is obtained from the study of cadaver anatomy. Some additional knowledge is secured from operative specimens and radiographic studies. Cholangiograms have added significant facts regarding the course and character of the common bile duct and its termination (9).

The present concept of the papilla of Vater has been based on many pretty pictures introduced in the past century. Certain thoughts concerning the end of the common bile and pancreatic ducts have been derived from observations often gleaned from necrotic specimens which were the site of massive enzymatic digestion. Present surgical attitudes towards the ducts' terminations have been formulated, in many cases, by palpation through a one centimeter-thick wall or after inexpert manipulation with a semi-rigid probe.

These ideas have been carried from text-book through manuscripts to other texts and have acted as fallacious premises for some illogical conclusions; this, too, in spite of some very excellent work (1, 2) presented during the 30's. These concepts were unfortunately engraved by "Opie" who observed a case of pancreatitis associated with a common duct stone (6).

Fallacious observations may yield inconsistent theories and procedures. An example of practical inconsistency is that the terms "papilla" and "ampulla" are interchanged. Etymologically, the "elevation" or "swelling," such as a "nipple," or the "papilla" should not be confused with the "dilated end" of a vessel, canal, or duct of an "ampulla." This is particularly interesting when it is realized that the "papilla" indicates a "mass" and the "ampulla," a "space." Just consider the implications when there is a lesion identified as "carcinoma of the ampulla" which could only be a malignant degeneration of a space.

It is true that there is an "ampulla" found in the embryo. It is seen in the formation of the "hepatopancreatic" duct. Early in its development, this primitive ampulla envelopes several openings into the duodenum. These channels arise through the coalescence of vacuoles following the nearly solid stage in the development of the duodenum (1).

This ampulla, at first, is co-extensive with the oblique intramural passage of the duodenum. Beginning at the 20 millimeter stage, the junction of bile and pancreatic ducts recedes from its window in the intestinal wall into the submucosa. At maturity of the embryo, this "ampulla" has involuted and a center of interstitial growth has expanded in the pre-ampullary segment of the ducts which forms the sphincters of Oddi (5). The embryonic ampulla does not (usually) exist beyond the duodenal submucosa (1).

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The major papilla varies in its location on the postero- or posteromedial duodenal wall. Ranges in distance from 55 to 142 millimeters have been reported (10) mostly from 80 to 120 millimeters from the pylorus. In 54 per cent of cases, the papilla is elevated above the surrounding mucous membrane. In 22 percent of cases, it is level with the surrounding duodenal mucosa. In 24 per cent of cases, the orifice of the common bile duct is visible in a depression surrounded by irregular ridges of duodenal mucous membranes.

It is obvious, then, that in 76 per cent of cases the papilla may be visible as a prominence. However, although in the remaining 24 per cent it is depressed, it is still composed of a solid mass of tissue.

Although the duct of Wirsung is medial and inferior to the common bile duct, that relationship is not maintained because the ducts intertwine. The termination of the pancreatic duct in 42 per cent of cases is almost directly inferior to the orifice of the common bile duct. The other 58 per cent of cases show a scattering in location of the exit for the pancreatic duct. It is significant, however, that if any plastic procedure be done, such as papillotomy or sphincterotomy, it is essential to identify the locations of pancreatic and common bile ducts.

The external appearance of the termination of the common bile duct is deceptive. To superficial examination, the duct diameter appears to increase distal to the apparent junction of the pancreatic and common bile ducts. This enlargement gradually decreases to a blunt ending within the duodenal canal.

However, sagittal section through the duct reveals that the increase in size seen externally is not an increase in lumen diameter, but is actually due to the increased width of the common duct wall. There is a decrease in the diameter of the lumen as the common bile duct crosses the duodenal wall.

The lumen of the pancreatic duct changes similarly but with not as much contrast because there is a smaller diameter and proportionately less (sphincter) muscle tissue.

The thickness of the duodenal wall varies from 3 to 12 millimeters. Its average thickness is five millimeters. By contrast, the papilla is from 7 to 19 millimeters in length, averaging 1.4 centimeters in length. At its widest axis, the diameter of the papilla ranges from 3.2 to 19.2 millimeters, averaging 6.8 millimeters.

It is important to realize such extensive variations in size. It is even more important to consider the disposition of the component elements of the papilla.

The transduodenal course of the common bile duct is transpapillary. In general, the duct, through this region, traverses a flattened "S"-shaped curve in at least two axes. The common bile duct enters the duodenal wall at somewhat less than a ninety degree angle. As it passes through the muscular layer of the duo-

denal wall, there is a slow curve present which generally parallels the longitudinal axis of the duodenal canal. At the termination of the common bile duct through the duodenal mucosa, the duct turns again to empty into the duodenum at nearly a right angle. The greatest decrease in diameter occurs in the proximal third of the transduodenal common bile duct.

Recent studies have been done on "cleared" specimens. In this type of investigation, there is no cutting of the papilla; the ducts are injected with a colored dye while all other tissues are rendered generally transparent to observation under the dissection microscope. In nearly forty per cent of cases, the common bile duct was completely separated from the pancreatic duct throughout the papilla. In forty-four per cent of cases, it is found that there is a "common channel" at the tip of the papilla. In the remainder of specimens (or about 16 per cent), a common channel is formed between the common bile and pancreatic ducts through at least fifty per cent of their transduodenal courses.

In these cases of the common channel which were observed in transparent specimens, it was found that in 70 per cent the common channel was in the distal third of the papilla. It was found that in 25 percent the common channel traversed the distal two-thirds of the papilla. In only 5 per cent (one case) did the common channel occupy more than two-thirds of the papilla.

It was significant that even in the presence of a "common channel" there was sturdy disposition of strong sphincter muscle proximally.

This can best be evaluated by cross-section study. Proximally, the two ducts are completely separated. Circumferential muscle and fibrous tissue totally surround the common bile duct; the pancreatic duct is loosely attached to the pericholedochal tissues by fine areolar and fibrous fatty tissue.

In the middle of the papilla, a rim of muscular and fibrous tissue surrounds each duct and also surrounds both of these sphincter muscles. The duct diameter begins to diminish as the extent of this muscle increases. Terminally, the ducts come together; the interductal muscle is gradually lost. At their tips only loose epithelial tissue is present.

Close observation of the duct lining reveals a sharp difference between the extraduodenal and transduodenal segments of the common bile duct.

The translucent membrane of the extraduodenal common bile duct is pock-marked with subtraction defects at about three or four per square centimeter. However, in the papillary portion, longitudinal and oblique striae and pleats are usually found. In most specimens (95 per cent), folds and reduplications are seen which look like "valvules." These are two to four millimeters long, one to two millimeters high, and less than one millimeter in thickness. They are irregular in axis and direction. The edges of one fold may merge with the midportion or edge of another. Many small folds can appear within a larger cusp. The arc of the valvule may point in either hepatic or duodenal direction. On microscopy, muscular and fibrous tissues were found extending from the wall of the duct in the "valvule" (8).

In this region of the common bile duct, several types of abnormalities have been observed. Among these are pancreato-ducto-choledochal fistulae and diverticula of the papilla (8).

The stone at the terminus of the common bile duct meets an impasse at the sphincter. The stone smaller than three millimeters can pass unless it is trapped. Under varying circumstances, the stone can become impacted, can penetrate through into the duodenum, or through into the pancreas.

A summary of over 1600 dissections (400 of mine) reveals that two orifices are seen in over 40 per cent of cases and that a common channel of less than the distal one-third of the papilla was present in about 37 per cent of cases. Anatomically speaking, less than 5 per cent of specimens were so constructed that the common channel traversed more than 70 per cent of the papilla. It was only under this last circumstance that reflux could be expected interductally.

Other studies have been done. In the patient, access to the common bile duct can be obtained only through surgery. In only a few cases can we be absolutely certain that the terminations of the duct were not traumatized. Under such conditions, results of cholangiograms may have to be partially discounted.

On the x-ray, the average length of the transduodenal segment of the duct is 14 millimeters. The lumen of the common bile duct decreases in diameter as it crosses the duodenal wall. Its sides have a double "concavity" or scalloping which gives the lumen the appearance of a "funnel." The duct finally terminates as a thin filamentous canal, the orifice of which measures approximately two millimeters in diameter (9).

There are other modes for study of the common bile duct and its termination. I have been particularly interested in studies of intracholedochal pressures and volumes. When sources for error have been considered, these observations are very significant. Essentially, we first determine residual pressure and volumes—then determine duct capacity, response to increased pressure and volumes, emptying rates of the duct, and patient symptom responses with relation to standard fasting and feeding conditions.

In summary, the following facts are available concerning the anatomy of the choledochus and its papilla of Vater:

1. The common bile duct pursues a constantly curving course.
2. The termination of the common bile duct in its transduodenal segment as the papilla of Vater
   (a) is like a funnel in that its lumen rapidly decreases in size (and rate of flow proportionately increases).
   (b) curves through a three dimensional route frequently intertwining with the pancreatic duct.
   (c) unites with the pancreatic duct to form an anatomic "common channel" in 50-60% of cases.

3. A common channel which traverses less than one-half to two-thirds of the papilla of Vater does not readily permit interductal reflux because of the anatomical disposition of the sphincter masses. Thus physiologic "common channel" exists only in approximately 5% of cases.

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PRELIMINARY EVALUATION OF A NEW DRUG, ANTRENYL. EFFECT ON GASTRIC SECRETION, MOTILITY AND RESULTS IN THE SYMPTOMATIC CARE OF PEPTIC ULCER

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IN THE medical treatment of peptic ulcer, much attention has been devoted to vagal depressants and anticholinergic drugs, presumably in the hope of accomplishing a medical vagotomy. Medical vagotomy, with its marked reduction in gastric motility and secretion could result in the cure of peptic ulcer in the absence of other therapeutic aids, such as diet, rest and antacids. Unfortunately all drugs studied to date have produced toxic symptoms before therapeutic vagotomy. As a result of this inability to achieve maximal therapeutic effects because of toxicity, they have either been relegated to the role of a therapeutic adjuvant in the general scheme of ulcer therapy, or have been dropped entirely from the therapeutic armamentarium.

Much has been written about the most time honored and perhaps still the most effective of these remedies, atropine (*2, 3, 12, 13, 14, 15, 20, 22*). Earlier writers such as Lockwood and Chamberlin, 1922 (15), Bolton, 1923 (2), reported only moderate reductions in gastric acidity with maximal clinical doses of this drug. In 1926 Keefer and Bloomfield (12) found that intramuscular therapeutic doses resulted in marked and sustained depression in the volume of gastric secretion, but that the effect on gastric acidity was much less pronounced. Similar results, indicating greater effect of atropine on volume than acidity, were reported by Porter (23). In 1933, Levin, Palmer and Kirsner (14) noted the inconsistency of the action of atropine on gastric secretion. They felt that no significant effect on gastric secretion occurs without side effects and that the clinical value of atropine is roughly proportional to the toxic effects of the drug.

Another parasympatholytic drug considered was dibutoline (17) which, when administered intramuscularly, depressed gastric secretions and motility and whose side effects were less severe and numerous than atropine. Because of its lack of effect when administered orally, this drug has not achieved widespread usage.

More recently quarternary amines have occupied a central position in the stage of clinical research.

Tetraethylammonium chloride (*1, 5, 7, 18, 29, 32*), although known chiefly for its vasodepressor effect, has also been found to reduce gastric motility and the volume and acidity of gastric secretion. It has been excluded, however, from the long term therapy of peptic ulcer because of extensive side effects.

Intramuscular hexamethonium (*6, 10, 11, 24*), likewise results in marked depression in gastric acidity and motility; it results in the suppression of the response of the gastric mucosa to insulin, although hyperchlorhydria due to histamine is not suppressed. Although clinical improvement in peptic ulcer has been described following intramuscular administration (chiefly due to its effect on gastric motility), side effects due chiefly to its vasodepressor action have limited its clinical usefulness.

In contrast to the above described quaternary amines, banthine has achieved a rather stable position as a therapeutic adjuvant in the management of peptic ulcer (*8, 9, 16, 25, 26, 27*). It is thought to produce its effect by parasympathetic neuroeffector blockade. Its influence on gastric motility is profound and prolonged; its effect on gastric volume is marked; its modifications of gastric volume and acidity are inconstant and variable. In the therapy of peptic ulcer, it results in prompt symptomatic relief and it is useful in the long term therapy of peptic ulcer, provided rest, diet, and antacids are included. In a comparative study by Benjamin, Rosiere and Grossman (4), it does not appear to be superior to atropine in its ability to reduce gastric secretion by the intramuscular route. As with atropine, marked therapeutic effects accompanying or comparable to those of medical vagotomy are precluded by toxicity.

The product under consideration, Antrenyl (diethyl

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(2-hydroxyethyl) methylammonium bromide α-phenylcyclohexaneglycolate), was submitted to us by the Ciba company for clinical investigation because of its atropine-like action, as discovered in preliminary animal investigations (28).

Methods and Results

In evaluating the effect of Antrenyl in peptic ulcer, three separate sets of studies were conducted:

(1) The effect of the drug by oral or intramuscular administration on volume, level of acidity; as compared with placebos and atropine.

(2) The effect of the drug on motility as compared with placebos.

(3) The effect of this new preparation on the clinical course of patients with peptic ulcer as compared with belladonna.

The need for control studies with placebos requires no explanation, as changes in gastric secretion, motility and symptoms have all been observed following placebos.

I. *Studies on Gastric Secretion*

a. *Methods.* All patients studied had been recently hospitalized for symptoms of uncomplicated peptic ulcer and had previous or current roentgen evidence of the disease. Any patient with previous surgery for peptic ulcer, recent symptoms of gastric retention, or signs of bleeding (including a positive stool guaiac test for occult blood) was rejected from the series.

The drug was given intragastrically and intramuscularly and compared with intragastric and intramuscular placebos as well as with intramuscular atropine.

For twenty-four hours prior to the test, all therapy other than rest and a soft bland diet was withheld. For six hours immediately preceding the test nothing by mouth was allowed.

A Levine tube was passed through the nose into the stomach until gastric secretion was obtained. Constant gastric aspiration was carried out by means of a Gomco suction machine set at a negative pressure of 120 millimeters of mercury. Secretions were obtained as separate samples every fifteen minutes. In those cases where the intragastric route was used, the medication (or its placebo likeness) was crushed in 15 cc. of water; the entire amount was injected through the Levine tube and flushed down with air. The tube was then clamped off for one hour to allow absorption. Subsequently aspiration was carried out for three to four hours. When the intramuscular route was used, continuous aspiration was employed for five hours after injection. To assure constant function of the aspiration unit, the apparatus and patient were watched continuously.

After one hour of constant aspiration each patient received one of the following:

Intragastrically:

Either Antrenyl (30 or 50 mg.) or a placebo

Intramuscularly:

Either 0.5 to 2.0 mg. of Antrenyl
or 0.43 or 0.87 mg. Atropine
or 1.0 cc. saline

Analysis of Specimens: At the end of the five hour period of aspiration the volume of each fifteen minute specimen was measured. The free and total acidity of the aspirate was titrated against a standardized sodium hydroxide solution employing Topfer's reagent (diethylamido-azo-benzine) and phenolphthalein as indicators. Degrees of acidity were calculated as the amount of 0.1 N sodium hydroxide required to raise the pH of 100 cc. of gastric juice to the end point of the indicators. Various conversion factors were employed as proper for the various concentrations of the solutions of sodium hydroxide actually used.

b. *Results.* In Table I are summarized average values for volume, free acid, and combined acid on three patients before and after receiving 2 mg. of Antrenyl intramuscularly and an equivalent volume of saline intramuscularly respectively on successive days. Determinations were carried out at fifteen minute intervals for four hours following injections.

TABLE I

EFFECT OF ANTRENYL I.M. VERSUS SALINE ON DIURNAL SECRETION

		Volume			Free Acid			Combined Acid		
		Before	After	% Change	Before	After	% Change	Before	After	% Change
Case 1	Antrenyl 2 mg.	26	14	−46	27	11	−59	20	18	−10
	Saline	21	22	+ 5	46	71	+56	29	39	+34
Case 2	Antrenyl 2 mg.	74	4	−95	32	2	−94	24	6	−75
	Saline	13	16	+23	15	10	−33	27	23	−15
Case 3	Antrenyl 2 mg.	49	6	−86	42	33	−21	22	21	− 5
	Saline	29	39	+34	19	11	−58	28	28	0

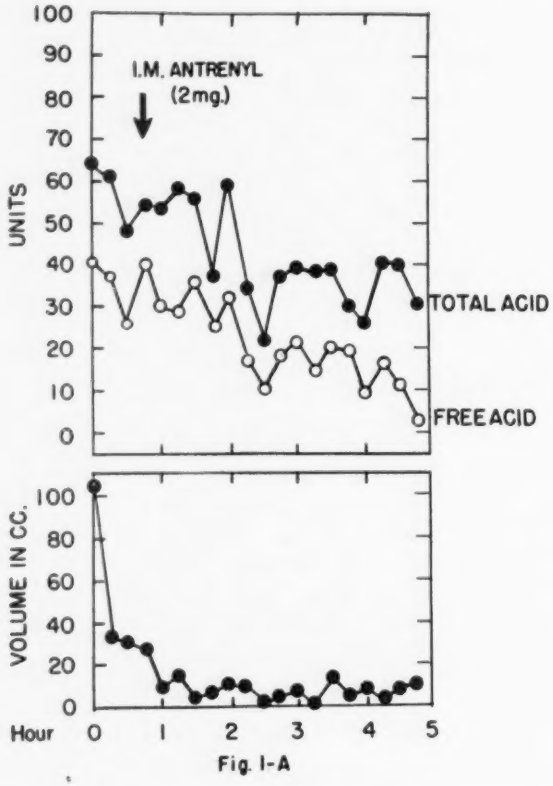

Fig. 1-A

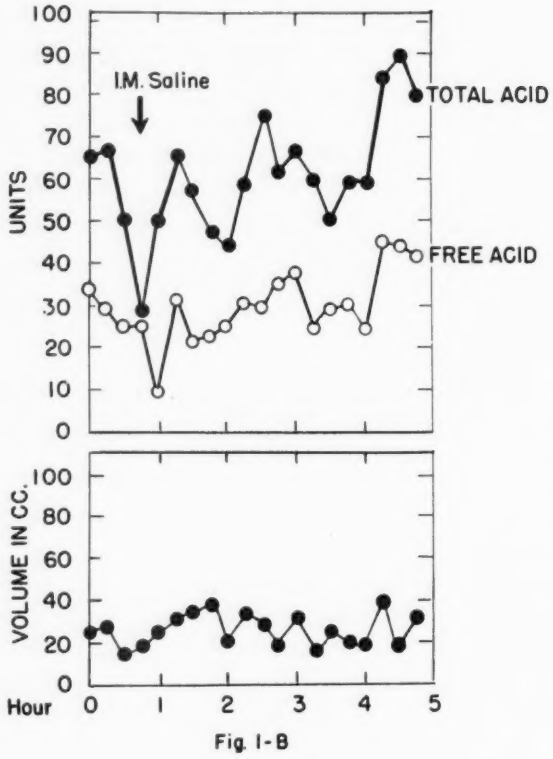

Fig. 1-B

It can readily be seen that the effect on volume is consistent and striking, that depression of free acids is marked, while combined acids exhibit more moderate effects.

Analysis of curves obtained by plotting individual results reveals prompt and well sustained declines in volumes, free acid and combined acid, during the entire period of observation as contrasted with wide fluctuations in all modalities after saline. The average curves are plotted in Figures 1a and 1b.

In Table 2 are recorded in similar fashion comparative effects of intramuscular Antrenyl and atropine. As can be readily seen, Antrenyl in 1.0 to 2.0 mg. doses intramuscularly caused consistent drops in volume, free acid and combined acid, while an 0.5 mg. dose affected volume only. There was no appreciable difference between the effects of atropine and Antrenyl in the doses used here. Toxic side effects of both drugs were of similar magnitude.

TABLE II

EFFECT OF ANTRENYL I.M. VERSUS I.M. ATROPINE ON DIURNAL SECRETION

			Volume			Free Acid			Combined Acid		
			Before	After	% Change	Before	After	% Change	Before	After	% Change
Case 1	Antrenyl	0.5 mg.	31	10	−68	14	30	+114	24	30	+25
	Antrenyl	2.0 mg.	5	2	−60	19	0	−100	20	12	−40
	Atropine	0.43 mg.	23	5	−78	46	47	+2	37	37	0
Case 2	Antrenyl	1.0 mg.	44	16	−64	32	11	−66	24	18	−25
	Atropine	0.87 mg.	54	14	−74	24	33	+37	23	23	0
Case 3	Antrenyl	1.5 mg.	38	9	−76	13	1	−92	23	10	−57
	Atropine	0.87 mg.	31	21	−32	12	2	−83	18	11	−39
Case 4	Antrenyl	2.0 mg.	13	2	−85	0	0	0	10	7	−30
	Atropine	0.87 mg.	13	0	−100	0	3		10	6	−40
Case 5	Antrenyl	2.0 mg.	20	2	−90	28	6	−79	27	17	−38
	Atropine	0.87 mg.	26	2	−92	22	1	−95	33	4	−88

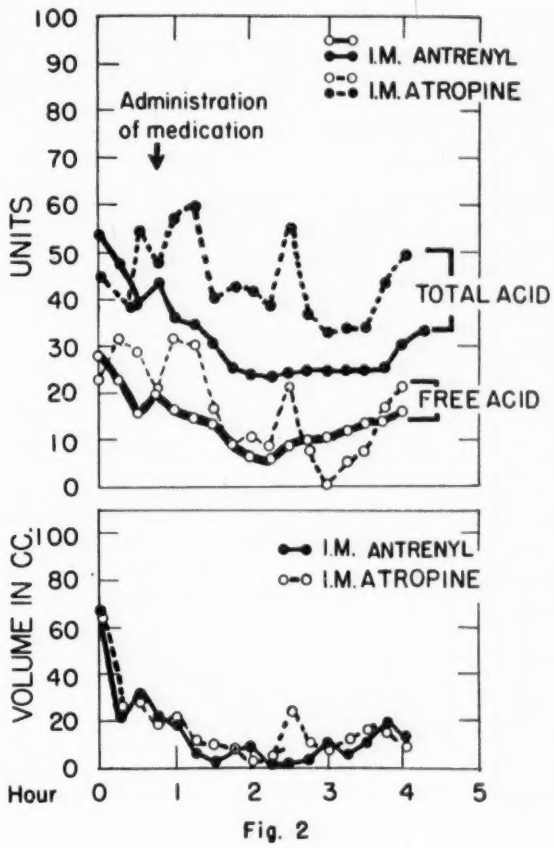

Fig. 2

A glance at Figure 2, showing average results for the five patients, shows dramatic and sustained changes with both drugs. Effects of Antrenyl on free and combined acids appear, from the graph, smoother and more sustained than those of atropine.

In Table 3 are shown effects on night secretions of oral Antrenyl (50 mg.) and placebos. Values were computed, starting one hour after intragastric administration of the drug and continuing every half hour for three hours.

TABLE III

EFFECT OF ORAL ANTRENYL VERSUS PLACEBOS ON NIGHT SECRETION

			Volume			Free Acid			Combined Acid		
			Before	After	% Change	Before	After	% Change	Before	After	% Change
Case 1	Antrenyl	50 mg.	65	11	−83	35	7	−75	17	18	+6
	Placebo		103	11	−89	8	10	+25	83	16	−81
Case 2	Antrenyl	50 mg.	77	7	−91	4	3	−25	8	21	+162
	Placebo		18	25	+39	4	1	−75	30	21	−33
Case 3	Antrenyl	50 mg.	23	2	−90	9	5	−44	21	10	−52
	Placebo		116	29	−75	0	24		2	35	+96
Case 4	Antrenyl	50 mg.	145	11	−93	50	24	−54	47	44	−6
	Placebo		60	31	−48	36	34	−6	84	65	−23
Case 5	Antrenyl	50 mg.	77	9	−88	58	15	−74	14	20	+43
	Placebo		40	30	−25	29	39	+27	42	25	−40

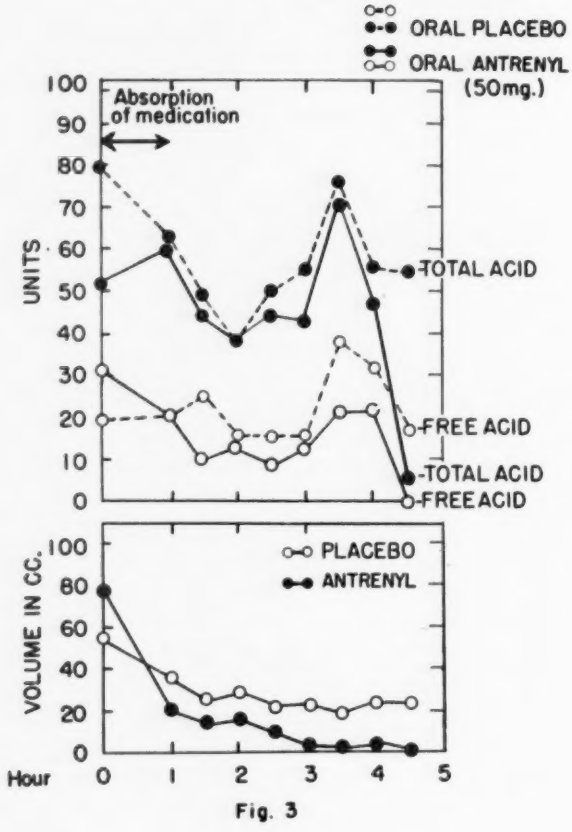

Fig. 3

As is apparent from Table 3, volumes show an excellent drop, free acids a quite respectable decline, combined acids a variable and inconsistent pattern. After placebo there were likewise drops in values of gastric secretion, but these were of lesser magnitude and less consistency than after oral Antrenyl. Acid values below ten are not considered since the percentage error is high here when dealing with a few units change; and also because obviously marked depression in acidity cannot be effected when minimal values exist initially.

Perusal of average curves in Figure 3 demonstrates fairly clearly the superiority of Antrenyl over placebos in the reduction of volume and free acid; however, total acids show no marked difference with Antrenyl. It should be emphasized at this point that because of toxicity these 50 mg. doses are somewhat too large for ordinary therapeutic purposes.

Table 4 summarizes studies conducted precisely as those in Table 2, except that these patients refused repeat studies, so that the effect of placebos could not be evaluated.

TABLE IV

EFFECT OF ORAL ANTRENYL ON GASTRIC NIGHT SECRETION
(No Placebos)

			Volume			Free Acid			Combined Acid		
			Before	After	% Change	Before	After	% Change	Before	After	% Change
Case 1	Antrenyl	50 mg.	37	37	+5	32	16	–50	28	33	+18
Case 2	Antrenyl	50 mg.	69	8	–90	23	19	–17	132	56	–58
Case 3	Antrenyl	50 mg.	72	1	–99	0	0	0	136	1	–99
Case 4	Antrenyl	50 mg.	43	16	–64	66	39	–41	55	45	–19
Case 5	Antrenyl	50 mg.	57	7	–87	0	5		39	18	–54

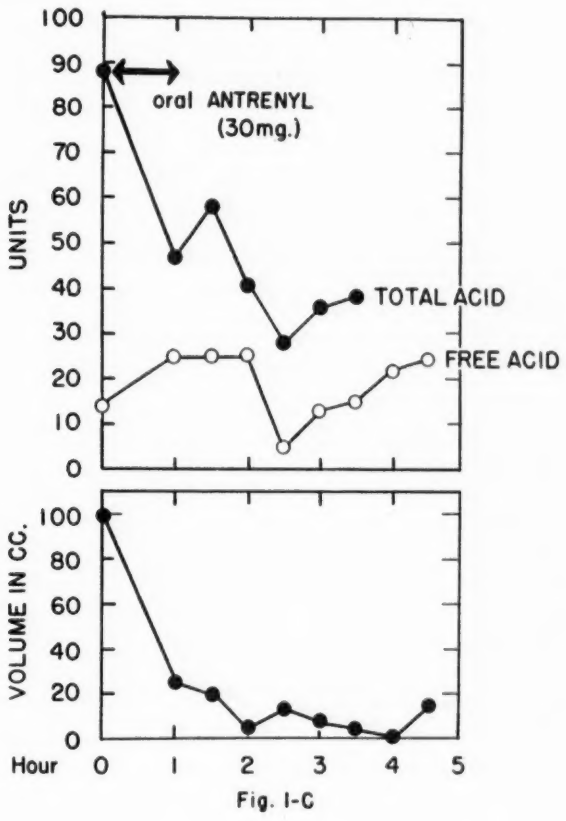

Fig. 1-C

Again, respectable drops were noted in volumes and in free acid. Response in combined acid, was as before, variable. These changes are not graphed.

Table 5 summarizes studies performed on three patients without controls using technics of observation similar to those in Table 3, except that these studies were performed in the morning instead of at night. The dosage of Antrenyl used here, namely 30 mg. by mouth, is acceptable for routine ulcer therapy.

TABLE V

EFFECT OF ORAL ANTRENYL ON DIURNAL GASTRIC SECRETION

	Volume			Free Acid			Combined Acid		
	Before	After	% Change	Before	After	% Change	Before	After	% Change
Case 1 Antrenyl 30 mg.	72	18	−75	8	35	+33	78	34	−57
Case 2 Antrenyl 30 mg.	35	4	−88	0	0	0	75	62	−17
Case 3 Antrenyl 30 mg.	64	14	−78	33	20	−39	77	26	−66

Here volumes were markedly reduced, results with free acid were inconclusive, combined acid showed a moderate drop. Detailed average values are graphed in Figure 1c.

II. *Studies on Gastric Motility*

a. *Methods.* In this group, five patients with demonstrated duodenal ulcer were given, on two separate days, 50 mg. of Antrenyl per os and a placebo, respectively, followed one-half hour later by the administration of 100 grams of Barium sulfate in 6 ounces of tap water. At hourly intervals, starting one hour after either placebo or Antrenyl, x-rays of the upper gastrointestinal tract were procured. Percentage of barium remaining in the stomach and the time for the head of the column of barium to reach the ileocecal junction were observed by a qualified radiologist, and are recorded in Table 6.

TABLE VI

MOTILITY STUDIES

Amount Barium Retained in Stomach

	1 hr.	2 hr.	3 hr.	4 hr.	5 hr.	7 hr.	9 hr.	10 hr.
Case O. N.								
Placebo	30%	10%	0% Barium in ileum	0% Barium in cecum				
Antrenyl 50 mg.	60%	50%	40%	30%	20%	20%	20% Rest of Ba. in terminal ileum	
Case P. C.								
Placebo	30%	0%	Barium at term. ileum	Barium in cecum				
Antrenyl 50 mg.	50%	not done	20% Barium not in ileum by 3 hrs.					
Case M. W.								
Placebo	50%	0% Barium at jejunum	0% Barium at cecum	0% Barium at ascending colon				
Antrenyl 100 mg.	100%	100%	100%	100%	100%	95% Barium in prox. jejunum	90%	85% Barium in prox. jejunum
Case P. N. C.								
Placebo	30%	15%	0% All Ba. in term. ileum & cecum					
Antrenyl 50 mg.	70%		50%		30%	30%	30% Ba. in jejunum & ileum	
Case L. W.								
Placebo	25%	10%	0% Ba. mostly ileum	0% Ba. mostly in ileum & cecum				
Antrenyl 50 mg.	50%	30%	20%	5-10%	*	**		

*At 5 hr. coating in antrum; barium mostly in ileum.

**At 8 hr. coating in ulcer crater and antrum; barium mostly in ileum and colon, to splenic flexure.

From the above table it is apparent that in this small series, 50 mg. doses of Antrenyl per os cause a marked reduction in motility. A 100 mg. dose literally stops the column of barium "in its track." All of the above doses were associated with toxic side effects, including chiefly dryness of the mouth and blurring of vision.

III. *Clinical Evaluation*

a. *Methods.* Antrenyl was given orally to patients with active, uncomplicated peptic ulcer in order to determine its effects on their signs, symptoms and nocturnal gastric secretions and to evaluate side effects.

The method of multiple alternates was used. Patients were selected by their hospital admission numbers; patients with odd numbers received 25 mg. of Antrenyl with a "tincture of belladonna placebo" every six hours, while those with even numbers received a placebo substitute for Antrenyl and 1.3 cc of genuine tincture of belladonna every six hours. All patients were told that they were receiving a "new ulcer drug" and tincture of belladonna. Usually the clinician evaluating the patient did not know which therapeutic regime was being employed. One of us (L. S.) was responsible for most of these observations.

On admission all patients were urged to maintain bed rest for forty-eight hours and were placed on a bland ulcer diet only. Sedatives, antacids, all other medications and between meal feedings were forbidden. If absolutely necessary, codeine was given to control pain until initial studies of night secretions were carried out.

Studies of night secretion were made for one to four nights immediately after admission, and were repeated after ten to fourteen days of therapy. They were carried out by passing a Levine tube into the stomach between 9 and 10 p.m. and then clamping the tube. Constant gastric suction was subsequently maintained from 10 p.m. until 5 a.m. by means of the Gomco suction apparatus as described previously. The apparatus was checked at least once an hour in an attempt to maintain constant function of the system. The aspirate was thoroughly mixed and measured for total volume. A sample was then titrated for free and total acidity as described under *analysis of specimens.*

After completion of initial night secretion studies, and after three to four days of hospitalization, treat-

ment with Antrenyl or belladonna was started as outlined. Three diets were prescribed as follows: No. 1 consisted of a soft bland feeding at 8 a.m., noon and 5 p.m.; No. 2 consisted of the three soft bland feedings with 240 cc. of milk at 12, 2, 4, 6 and 10 a.m.; No. 3 consisted of milk only, every hour from 7 a.m. until 10 p.m. and at 12, 2, 4 and 6 a.m. All patients were maintained on diet No. 1 until initial night secretion studies were completed. Then, if in the opinion of the clinician, symptoms were so severe that more vigorous therapy was mandatory, the patient was placed on diet No. 2 or No. 3 as was indicated by the severity of symptoms. Diet No. 2 was also administered to patients who had treatment for ten days and who, in the opinion of the clinician, did not show significant improvement. Patients were continued on the stricter regimes until they were asymptomatic for seventy-two hours. Then they progressed to the less strict diet.

While hospitalized, the patients were evaluated daily for: the presence of ulcer type discomfort, its duration and frequency; the occurrence and duration of night pains; the presence of epigastric tenderness; urinary frequency; nocturia and hesitancy; the number of spontaneous bowel movements every twenty-four hours; and for the presence of xerostomia, cycloplegia and dizziness.

b. *Results.* After eliminating ten patients for various reasons, including poor cooperation, toxic side effects from drug and the development of gastrointestinal bleeding, twenty-two individuals remained in the series (eleven on Antrenyl, eleven on belladonna).

Examination of data showed that the two groups (Antrenyl versus belladonna) were similar in most respects, as is demonstrated by the tabulation below:

	Antrenyl Group	*Belladonna Group*
Age average	39	38
range	23-74	25-63
Number of patients previously hospitalized for peptic ulcer	5	6
Previous x-ray findings	6	8
Previous therapy	8	9
Average duration of symptoms (with few exceptions)	57 mo.	46 mo.
Marked pylorospasm	1	2
Ulcer craters	2	7
Simple duodenal deformity	8	2

One difference between the group concerned the initial x-ray picture with predominance of ulcer craters in the belladonna group. It may be stated that x-rays could never be obtained prior to the tenth day after admission.

Symptomatic changes effected are compared in Table 7. Toxic side effects with the two drugs are summarized in Table 8.

TABLE VII

SYMPTOMATIC EFFECTS

DAY OF HOSPITALIZATION		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Average duration of pain per patient in hours	Be*	12	9	8	7	5	4	3	2	3	4	3	4	5	4	2	2	4	3	2	2
	Ba**	12	7	6	7	3	3	3	2	1	1	2	0	0	0	0	0	0	0	0	0
Frequency of pain	Be	11	9	10	11	7	12	5	6	5	7	7	7	10	5	4	3	8	6	3	2
	Ba	13	17	14	9	8	8	8	5	4	4	3	2	1	0	0	0	0	0	0	0
Average duration of night pain in hrs./pt.	Be	6	5	3	3	4	3	2	2	3	2	4	1	2	2	1	0	2	2	2	0
	Ba	4	4	2	2	2	2	1	0	1	1	2	0	0	0	1	0	0	0	0	0
No. of patients with epigastric tenderness	Be	9	9	8	7	7	6	5	5	3	4	3	3	3	2	2	1	1	1	1	1
	Ba	9	9	9	8	6	4	6	5	3	3	1	0	0	0	0	0	0	0	0	0

*Belladonna
**Antrenyl

TABLE VIII

TOXIC SIDE EFFECTS

DAY OF HOSPITALIZATION		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Average urinary frequency per patient	Be*	4	4	4	4	4	4	4	4	5	4	4	4	4	5	5	4	4	4	4	4
	Ba**	4	4	4	3	4	7	7	6	5	6	6	6	6	5	5	4	4	4	4	4
Number of patients with hesitancy	Be	0	0	0	0	1	2	4	3	3	3	2	2	2	2	2	2	2	2	4	3
	Ba	0	0	1	3	5	10	11	10	8	8	8	7	6	6	6	6	6	6	6	6
Occurrence of nocturia	Be	3	3	3	5	5	4	9	7	7	7	6	6	6	3	4	5	4	3	3	4
	Ba	5	1	5	6	9	15	13	3	8	7	9	7	3	5	6	1	5	7	7	6
Bowel movements per 24 hrs.	Be	7	7	7	6	9	7	7	3	6	8	11	6	8	10	7	6	8	9	11	8
	Ba	8	6	12	11	4	6	1	2	2	2	3	4	4	5	5	3	7	7	6	5
Number of patients with dry mouth	Be	0	0	1	0	2	2	6	9	9	7	8	8	8	6	6	6	7	7	7	7
	Ba	0	1	2	6	9	11	10	11	10	10	10	10	10	9	11	9	10	9	10	10
Number of patients with blurred vision	Be	0	0	0	0	1	2	6	6	6	7	7	7	7	6	9	10	9	9	8	7
	Ba	1	1	3	6	9	10	9	10	10	10	9	9	9	9	9	10	9	8	8	7

*Belladonna
**Antrenyl

It is evident from the above tables that oral Antrenyl resulted in more rapid symptomatic relief than belladonna, but that its side effects are more pronounced in the dosages used.

The effects of atropine and Antrenyl on night secretions before and after ten to fourteen days of therapy are listed in Table 9. It should be emphasized that medication was carried without interruption until the final samples of night secretion were drawn.

TABLE IX

THE EFFECTS OF ATROPINE AND ANTRENYL ON NIGHT SECRETIONS BEFORE AND AFTER 10 TO 14 DAYS OF THERAPY

ATROPINE

Volume		Free Acid		Total Acid	
Before	After	Before	After	Before	After
675	962	50	59	86	104
700	268	14	27	44	91
300	337	59	76	89	104
150	540	27	51	39	118
201	360	16	15	40	47
750	941	35	46	96	127
503	333	31	21	71	73
137	150	29	7	87	117
167	550	54	35	71	68
92	350	33	37	12	65
625	275	58	41	90	53
436	461	32	38	66	88

ANTRENYL

Volume		Free Acid		Total Acid	
Before	After	Before	After	Before	After
437	75	31	27	92	61
648	120	36	34	58	48
175	187	13	38	50	69
....	....	....	....	....	....
445	580	15	17	39	78
375	100	58	22	90	62
450	100	39	0	61	17
301	173	24	31	48	76
512	225	33	28	78	64
310	400	....	....	....	....
575	183	39	32	63	75
423	214	32	25	65	61

It is apparent from Table 9 that the long term effects of oral Antrenyl or atropine on night secretions are very slight, the only significant change being a 50% drop in average volumes after Antrenyl.

Discussion

Much attention has been directed to vagal depressants because of their potential, but as yet unrealized, ability to produce medical vagotomy. Ciba's Antrenyl has been investigated with this possibility in mind. There were three phases in the present study, (1) Effect of Antrenyl on gastric secretion, (2) Effect on gastric motility, (3) Clinical results.

All studies were conducted with controls to circumvent the effects of such intangibles as reassurance, rest, diet, and increased security attending hospitalization. In the studies on gastric secretions and motility, controls and actual studies were performed by the same observers at the same time of the day and in entirely similar environment.

The results of intramuscular Antrenyl injections showed striking effects in volume, free acid and combined acid of gastric secretion in doses above 1 mg., especially when contrasted with saline. The single observation on the effect of 0.5 mg. intramuscularly showed depression of volume with no effects on acids.

Intramuscular injections of Antrenyl (1 to 2 mg. doses) and of atropine in 0.43 to 0.87 mg. amounts revealed little difference in their effects on gastric secretion, although both results were striking; in fact, results obtained here with atropine appear more definite than those described in the medical literature at large.

Results with oral medication, whether in 30 or 50 mg. doses, show marked reduction in value as compared with placebos. There is apparently little difference in the results in free acid and combined acid between drug and control studies. If, however, only those free acid changes are included which start from a fair sized initial value (10 degrees or more) effects on free acids are apparently better than after placebos.

Effects of oral medication on motility are uniformly striking as compared with controls, even using the fairly crude and insensitive method of analysis of studying by x-ray the transit of barium through the gastrointestinal tract. This marked effect may perhaps explain superior symptomatic relief using this medication as contrasted with belladonna.

The clinical study has one obvious weakness, namely the greater number of craters in control patients as compared with those on Antrenyl. G. I. series, unfortunately, could only be obtained on the average ten days after admission, so that craters might have healed in certain cases in that time (perhaps in more cases on Antrenyl than on belladonna).

Only symptomatic effects were noted. It was not possible to follow these patients for healing on a long term basis, because they usually deviated from the strictly controlled regime of the hospital as soon as they were discharged.

Symptomatic relief was prompter with Antrenyl than with belladonna. Side effects were greater with Antrenyl than with belladonna. The question naturally occurs whether belladonna would have been equally effective in doses pushed up to equally toxic levels.

Long term effects on gastric night secretion appear insignificant in both groups except for the effect on volume after Antrenyl. These slight effects which result with continued therapy of Antrenyl are in contrast to those immediately following ingestion of the drug. They would tend to indicate that there is no long term cumulative effect on gastric secretion of this preparation, and that continued administration of the drug, with its transient effects following each dose, is required.

Conclusions

Antrenyl has been studied because of its atropine like effect, with the hope that unlike its predecessors,

atropine, dibutoline, banthine, etc., toxicity would not preclude medical vagotomy.

While it falls short of this ideal, our brief study reveals striking and useful properties: When used by the intramuscular route it depresses volume, free acid and combined acid of gastric juice at least as well as atropine. By the oral route, in 30 to 50 mg. doses, it suppresses volume, reduces free acids, but does not consistently modify combined acids. Its effect on motility in oral doses is striking and perhaps accounts for its superiority over belladonna in relieving symptoms of peptic ulcer.

From this all too brief study twofold therapeutic uses are suggested. (1) In the symptomatic relief of acute ulcer symptoms, (2) In the long term treatment of peptic ulcer, provided it is administered in conjunction with known antacids such as Amphojel, Carmethose or Creamalin. These could completely neutralize secretions, whose volume and free acids have already been reduced by Antrenyl. Marked reduction in motility would help assuring prolonged retention of these antacids within the stomach and a lengthening of the period of contact with gastric juices.

Final evaluation of this new compound awaits the accumulation of much more extensive data regarding its pharmacological and clinical effects.

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CALCIFIED CYST OF THE PANCREAS

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THERE ARE numerous reports in the literature on the subject of pancreatic cysts. However, calcification in the cyst wall is comparatively uncommon. Occasionally, calcification is found in the following types of pancreatic cyst; echinococcus, dermoid and pseudocysts incident to trauma. Although infestation by Taenia echinococcus may be encountered in any part of the world, it is found most frequently in Australia, South America, Greece, Rumania and Italy. In 1939, Paraskevas (13) reported that there were one hundred and four recorded cases of echinococcus cyst of the pancreas. Dermoid cysts of the pancreas are very rare. Dennis (6) described a dermoid cyst in a male patient forty years of age. A flat plate of the abdomen revealed calcification in the cyst wall and at operation a considerable amount of calcareous deposit was found in the lining. DeCourcy (5) in 1943 reported a dermoid cyst in a two year old, female infant and a survey of the literature at that time revealed only two other such cases. The most common cystic lesion of the pancreas is the pseudocyst. These lesions are not true cysts and arise outside of the substance of the gland. They do not have an epithelial lining. In most instances, such cysts are the result of trauma to the upper abdomen and acute or chronic pancreatitis. Calcification is the result of inflammation, necrosis, hemorrhage or infection. In the acute state of pancreatitis, there has been found a high calcium content in the gland, which probably forms a nidus for further deposition until sufficient accumulates to produce radiological evidence (14). However, roentgen findings (3, 8) indicate that calcium deposits rarely outline the cyst wall.

Fig. 1: Roentgenogram of abdomen showing large, partially calcified mass in the left upper quadrant.

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CASE REPORT

C. L., a fifty-four year old white male was admitted to the hospital in July 1952 for possible cataract surgery. Diabetes mellitus was diagnosed in 1928. With insulin and an adequate diet he had maintained a fair degree of control during this twenty-four year period. There was one episode of diabetic coma in 1933. On admission to the hospital he was taking thirty-five units of NPH insulin daily before breakfast. About five years ago, a vitreous hemorrhage occurred in the right eye with resulting loss of vision. Shortly thereafter, the left eye was similarly affected. During the past two years cataracts developed in both eyes. Past history of trauma was significant in that about eight years ago he sustained a severe kick to the upper abdomen.

Examination revealed bilateral cataracts with vision limited to light perception only. The blood pressure was 138/78 and oscillometric readings of the lower extremities were reduced. On palpation of the abdomen a grapefruit-sized mass was found in the upper ab-

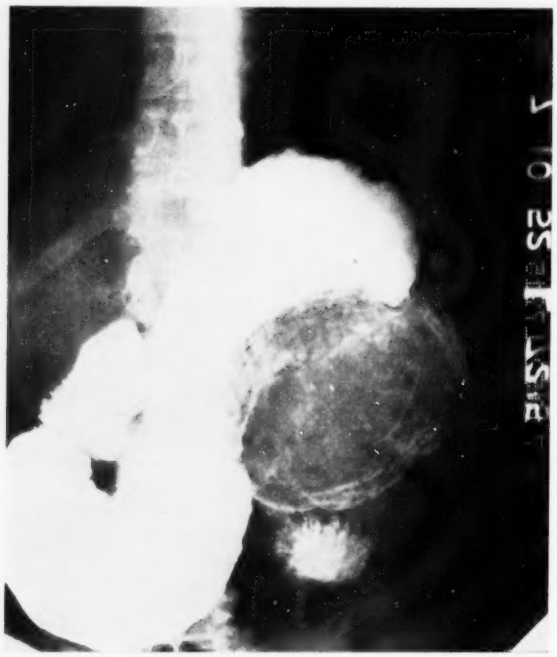

Fig. 2: Roentgenogram showing indentation of the greater curvature of the stomach.

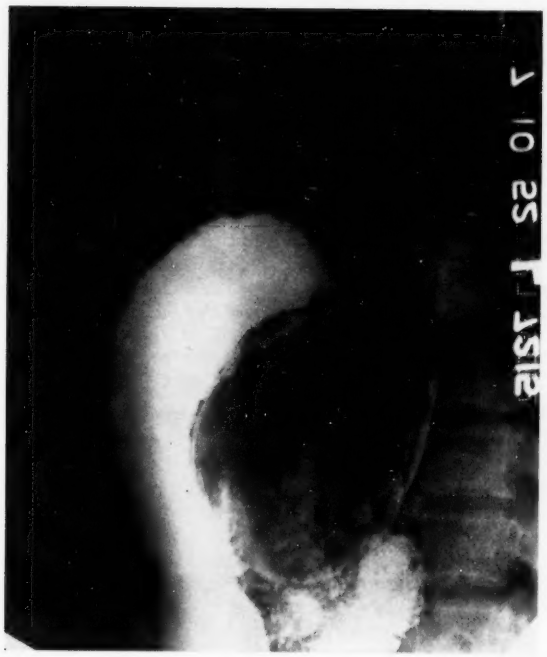

Fig. 3: Lateral view showing anterior displacement of the stomach.

domen to the left of the midline. It was firm and not freely movable or tender.

Blood chemistry included glucose values of 124, 238 and 186. Blood counts showed a hemoglobin of 13.7 grams, erythrocytes 4,210,000, leucocytes 5,900 and a normal differential. Urinalysis was negative except for a trace of albumin and occasional glycosuria. A roentgenogram (figure 1) of the abdomen revealed a large, partially calcified ovoid mass in the left upper quadrant measuring approximately 10 by 15 cm. Barium meal studies (figure 2) showed indentation of the greater curvature of the stomach and displacement of the gastric shadow to the right. A lateral view (figure 3) during barium meal examination showed anterior displacement of the stomach.

COMMENT

There is experimental (10) and clinical evidence of the role of trauma in the production of pseudocyst of the pancreas. In most instances the injury is that of a severe blow or crushing force to the upper abdomen probably producing compression of the pancreas against the first lumbar vertebra. There was a history of abdominal injury in 33 of 117 cases recorded by Körte (9). On review of the literature in 1943, Harrison and Cooper (7) found fifty-one cases of pseudocysts of the pancreas which presumably were the direct result of trauma. A history of trauma was elicited in sixteen of thirty-one cases studied by Meyer, Sheridan and Murphy (11). In addition to trauma it has been established that acute inflammatory conditions of the gallbladder and pancreas are causative factors in the development of pancreatic cysts.

Norman (12) recently reported a cyst of the pancreas associated with diabetes mellitus and stated that this association was rarely found. However, cystadenoma of the pancreas with diabetes is not infrequent. A review of the literature in 1947 by Benson and Gordon (1), revealed that six of twenty-eight surgically explored cases had diabetes preoperatively. It was their opinion that the diabetic state did not result from destruction of pancreatic tissue by the tumor. Bowers et al (2) encountered diabetes in three of five patients with cystadenoma of the pancreas. In one instance, the diabetes was less severe following surgery.

Occasionally, the outline of a pancreatic cyst may be clearly visible in a roentgenogram of the abdomen. Generally, the diagnosis depends on the pressure defects produced by the cyst on the barium-filled stomach, proximal small bowel and colon. The roentgen findings depicted in the subject of this report are typical of a cyst arising from the tail of the pancreas. Case (4) and others have demonstrated that such a lesion frequently produces a smoothly rounded indentation in the greater curvature of the stomach at or just above its midportion. Lateral views reveal anterior displacement of the stomach with indentation of its posterior wall.

SUMMARY

A case of calcified cyst of the pancreas in a diabetic is reported. The presence of calcification in pancreatic cysts, associated diabetes mellitus and etiological factors have been discussed.

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SPONTANEOUS HYPOGLYCEMIA IN ACUTE GASTRO-ENTERITIS

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THE RELATIVE constancy of the normal blood sugar level in the fasting state represents a remarkable physiological phenomenon. When sugar is not being absorbed from the intestinal tract, such as in fasting or vomiting, an emergency supply of liver glycogen becomes available for gluconeogenesis. It has been estimated that approximately 100 grams of glycogen are present in the liver of the healthy individual and this would only supply the demands for sugar for some five hours (1). Further demands must be met from non-carbohydrate sources of the body under the control of the internal secretions of the pituitary, the adrenal cortex, and the pancreas. Thus, the maintenance of the normal blood sugar during fasting becomes a complex mechanism depending on chemical, nervous, and humoral factors.

A defect in the homeostatic control of the blood sugar level may not make itself clinically manifest unless the demands for a normal blood sugar level are particularly great such as during vomiting, fasting, fever, or dehydration. If the resulting hypoglycemia is not recognized, it may greatly add to the hazard of the primary disease and if not corrected may prove detrimental.

It is such a case that is herewith presented.

CASE REPORT

Mr. S. V. aged 40 was admitted to the Michael Reese Hospital on March 29, 1952, with a history of epigastric distress, nausea, and vomiting of three days duration. Bed rest, dietary measures, and medication failed to relieve his condition. Pain and emesis increased in intensity. For the past 24 hours the patient has been unable to retain solid or liquid food.

Physical examination disclosed the patient in acute distress. There was obvious dehydration with dryness of the mucous membranes and diminished turgor of the skin. The face was flushed, the temperature was 97.8 degrees, the pulse rate was 76, the respiratory rate 20, and the blood pressure 118 systolic over 78 diastolic. There were no significant cardiac or pulmonary findings. The abdomen was moderately distended and soft. Bowel sounds were audible. There was diffuse mid-epigastric and periumbilical tenderness without rebound tenderness or muscular spasms. The remainder of the physical examination was essentially negative.

Because of the acute state of dehydration, 1000 cc. of 10% glucose in saline were immediately administered by intravenous clysis. Meanwhile, essential laboratory tests were performed revealing a red blood cell count of 4,710,000, 13.8 grams % hemoglobin, a white blood cell count of 10,300, a differential count of 52% polynuclear, 28% lymphocytes, 2% eosinophiles, and 8% monocytes. The hematocrit was 45%, the sedimentation rate was 34mm. The urine examination was normal.

When seen the next morning, the patient appeared distinctly worse. He perspired profusely and his face was flushed. There was considerable dyspnea. The cardiac rate was 120, rapid and regular. No murmurs were heard. The patient complained of a feeling of impending disaster. Attempts toward oral feedings had failed and were followed by profuse vomiting.

A blood sugar taken at this time was 55 mgm%. The urea N was 16 mgm%, cholesterol 109 mgm%, cholesterol ester 69%, amylase 99 units. Because of the evident hypoglycemic state, the patient was immediately given another intravenous infusion of 10% glucose in saline solution. The response was immediate and the patient was soon able to retain sweetened fluids by mouth. At the next morning, however, another hypoglycemic episode occurred after no food had been given during the night. The blood sugar at this time was 48 mgm%, chlorides 104 m.e./L, CO_2 22 mM/L, sodium 135 m.e./L, potassium 3.7 m.e./L. Intravenous glucose was again administered with prompt improvement of the patient's status.

It appeared evident that some breakdown in the patient's blood sugar regulatory mechanism had taken place. Accordingly, the following test was performed: no food was given after midnight, blood sugar determinations were performed at half hour intervals beginning at 8 a.m. The results were as follows: 58, 65, 80, 82, 85, 79, (in mgm%). While the patient was closely observed during the test for recurrent hypoglycemic attacks, he felt remarkably well. Subsequently, rapid and continuous improvement took place. Epigastric distress and vomiting subsided. Food was well tolerated. The patient felt stronger and became asymptomatic. He was discharged on the 6th hospital day. At a later date, X-rays of the gastro-intestinal tract and the gallbladder, stool examinations, and liver function tests disclosed normal findings throughout.

COMMENTS

Spontaneous hypoglycemia in acute gastro-enteritis is an unusual event. It is not mentioned in the etiology and classification of the hypoglycemias (2). Vomiting, fasting, anorexia, and dehydration should increase the tendency to hypoglycemia. It would seem surprising that it does not occur more frequently in acute gastric disturbances. It may be that slight hypoglycemic episodes are overlooked unless specifically searched for, or it may be that a considerable breakdown in the homeostatic mechanism for blood sugar control has to occur before such marked hypoglycemia, as observed in our case, becomes manifest.

Clinical and laboratory investigation as to the cause of the hypoglycemia in our case failed to demonstrate evidence of an organic lesion of either pituitary, thyroid, pancreas, or liver. A rising blood sugar curve

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Submitted Nov. 8, 1952.

during a period of fasting, tended to exclude pancreatic island adenoma as an etiologic factor and pointed to some compensatory mechanism on the part of the pituitary-adrenal system.

In the absence of demonstrable anatomical lesions there continues to be speculation concerning the etiology of "functional" hypoglycemia. Low blood sugar values found in nervous, tense, and neurotic individuals are considered a form of functional hyperinsulin according to Conn (3). Portis (4) describes a well defined group of psychoneurotic patients in whom hypoglycemia appeared to be due to hyperinsulism resulting from vagus stimulation. Apparently, emotional processes are being relayed through the hypothalmus to the autonomic nervous system resulting in neurogenic hyperinsulinism. Depressive states, anxiety states, such as may occur during sickness, can be accompanied by manifest hyperinsulism (5).

Whatever the cause of such lability in the glucose regulatory mechanism may be, it seems well conceivable that such a state may exist in a subclinical form to become manifest only when stress situations or organic inability to take food exists. If such a possibility is kept in mind, an acute hypoglycemic attack can readily be recognized and treated accordingly.

It is for this reason that attention has been called to the case described.

SUMMARY AND CONCLUSIONS

Acute hypoglycemic episodes complicating an acute attack of gastro-enteritis subsided readily with improvement of the underlying disease. In the absence of an organic cause for hypoglycemic attacks, it is suggested that functional hyperinsulism may exist in a subclinical form to become manifest during a period of mental stress and organic inability to take food.

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ABSTRACTS ON NUTRITION

SIPERSTEIN, M. D., NICHOLS, C. W. AND CHAIKOFF, I. L.: *Prevention of plasma cholesterol elevation and atherosclerosis in the cholesterol-fed bird by the administration of dihydrocholesterol.* Circulation, VII, I, Jan. 1953, 37-41.

Birds fed a diet containing 1 percent cholesterol developed characteristic lipemia with average plasma cholesterol values ranging from 665 to 948 mg. per 100 ml. during the 11 month period of the experiment. Simultaneous feeding of dihydrocholesterol with the 1 percent cholesterol diet resulted in complete suppression of the lipemia. During the period of observation the average plasma cholesterol values varied from 120 to 179 mg. per 100 ml. In control birds fed a stock diet containing no cholesterol, average values for plasma cholesterol ranged from 101 to 147 per 100 ml. The development of atherosclerosis in the cholesterol fed birds was greatly inhibited by the simultaneous administration of dihydrocholesterol. Indeed, no measurable difference was noted in the extent of atherosclerosis between birds fed the control diet and those fed cholesterol plus dihydrocholesterol. The latter appeared to act as a "blocking" agent.

KILNESS, A. W.: *Heavily nitrated water, methemoglobinemia and adrenal tumors as found in a family with multiple endocrinopathies.* Am. Pract. & Dig. Treat., 4, 1, Jan. 1953, 45-47.

Two infants with malnutrition, cyanosis and dyspnea are described, one of which died with methemoglobinemia and an associated adrenal neuroblastoma. The mother has a chronic discoid lupus erythematosis with photosensitivity. A son, aged 10, shows signs of premature virilism, anemia, intermittent cyanosis, bouts of mental aberration and had an enlarged thymus gland at birth. The well-water used by the family showed a toxic concentration of 125 parts per million of nitrates. No conclusions are, or can be, drawn from the peculiar data presented.

LAL, S. B.: *Dietary study of agricultural landless laborers of Bhabhua (Bihar).* J. Indian Med. Assn., XXII, 3, Dec. 1952, 101-105.

The dietary habits of farmer-owners, farm workers, and professional persons in Bhabhua were investigated to ascertain if the foods eaten by these 3 social classes were adequate. This particular area was selected, however, because the people here are in the habit of eating raw, home-pounded (not milled) rice and it seemed advisable to find out if this food, which accounted for a high percentage of the total calories, exerted any ill-effects on health. Briefly, it was found that there was no evidence of lack of thiamine. Even as little as 35 percent of the thiamine in the raw rice would have been sufficient to prevent deficiency. The chief lack in the diets of these people was animal protein and calcium. Only a small percentage of the children showed evidence of nutritional disease and they were well nourished in comparison with those surveyed in some of the other areas of the state.

WILENTZ, W. C.: *The alcohol factor in violent deaths.* Am. Pract. & Dig. Treat., 4, 1, Jan. 1953, 21-24.

The author shows that over a period of 19 years, ethyl alcohol was a contributing or responsible factor in 37 percent of 1258 cases of violent deaths. In this

group, 206 were intoxicated, while 259 had been drinking. The drunken condition usually led to a fatal traumatic accident. As Wilentz correctly says, the amount of alcohol consumed by Americans is a national disgrace. Three times more liquor is consumed in Washington, D. C. per capita than in the rest of the nation. The author believes it is time "to give this disgraceful performance of instability and bad manners very serious consideration."

LIBRACH, I. M.: *Toxic reactions due to intravenous iron.* Brit. Med. J., Jan. 3, 1953, 21-24.

The author describes toxic reactions to the intravenous administration of iron and wisely states that "iron is a dangerous drug." The most of the paper is an attempt to explain the toxicity of intravenous iron. The iron forms a compound with the globulin of the blood, and reactions may be due to an allergy to this compound. In some cases death may result, due, apparently, to a wide-spread interference with cell function, on an anaphylactic basis.

HARRIES, J. M. *and* HOLLINGSWORTH, D. F.: *Food supply, body weight and activity in Great Britain, 1943-9.* Brit. Med. J., Jan. 10, 1953, 75-78.

The average changes in weight of groups of industrial workers (male and female) in small firms and of housewives measured during the course of the Ministry of Food's "Body Weight Survey, 1943-9," have been compared with the caloric value of the food consumption recorded for urban working class households in the Ministry's National Food Survey during the same years. Body weights of adults fluctuated with the caloric value of the diet. The growth rates of children probably show a similar variation. It appears that body weight can be used as an earlier index of inadequacy in food supplies, than clinical examinations.

MAY, C. D., STEWART, C. T., HAMILTON, A. AND SALMON, R. J.: *Infection as cause of folic acid deficiency and megaloblastic anemia: experimental induction of megaloblastic anemia by turpentine abscess.* Am. J. Dis. Child., 84, 6, Dec. 1952, 718-728.

The authors describe the spontaneous occurrence of megaloblastic anemia in association with infection in infants and monkeys. Megaloblastic anemia was induced experimentally in monkeys by producing sterile abscesses with intramuscular injections of turpentine. The low content of folic acid compounds in the liver in both natural and experimental infections and the elimination of megaloblasts from the marrow by folic acid, but not by vitamin B_{12} or ascorbic acid, leads to the conclusion that infection can cause a deficiency of folic acid compounds. In cases of severe or prolonged infections in infants, it would be wise to include additional amounts of vitamin B_{12} and folic acid in the treatment during the infection and the immediate convalescent period.

STEWART, C. T., SALMON, R. J. AND MAY, C. D.: *Factors determining effect of insulin on metabolism of glucose in ascorbic acid deficiency and scurvy in the monkey.* Am. J. Dis. Child., 84, 6, Dec. 1952, 677-691.

This study was undertaken to determine the effect of ascorbic acid deficiency on adrenocortical function. The effect of insulin on the level of blood glucose was chosen as a test of adrenocortical function. It was found that the dose of insulin which produced a pronounced depression of blood sugar in control monkeys had little effect in scorbutic monkeys. Experiments were performed analyzing the influence of epinephrine and cortisone on the response to insulin in scurvy. The data obtained indicate that adrenocortical function is increased in scurvy rather than decreased and that this accounts for the relative lack of effect of insulin on blood sugar in scurvy.

MEERLOO, J. A. M. AND KLAUBER, L. D.: *Clinical significance of starvation and oral deprivation.* Psychosomatic Med., XIV, 6, Nov.-Dec. 1952, 491-497.

Patients with semistarvation and oral deprivation on the basis of organic disease or following operations may develop psychological symptoms which in turn aggravate the disease or paralyze the wish to live. Any patient who is strenuously dieted may masochistically surrender to the therapist and become extremely miserable. Consequently it is often a question whether a strict diet may not do more psychological harm than physical good.

JELLIFFE, D. B.: *The protein content of the breast milk of African women.* Brit. Med. J., Nov. 22, 1952, 1131-1132.

76 specimens of breast milk from Nigerian nursing mothers were analyzed to determine the protein content. The average was found to be 1.04 percent. The length of lactation varied from 1 to 36 months. No evidence was found of a decrease of the protein content with prolonged lactation. The results compare favorably with those from other parts of the world. The research was done because a few infants develop kwashiorkor while still on breast milk.

WHELAN, W. J. AND WHITAKER, D. A.: *A new South African beverage plant, Helechrysum nudifolium Less. var. Quinquenerve (Thunb.) Moes.* S. Afr. J. Med. Sci., 1952, 17, 77-8.

The leaf of the plant referred to in the title is used as a tea by Europeans and Africans in the Barberton District since 1900. The leaf is nontoxic, contains neither alkaloid nor glucoside, but yields a trace of tannins and 0.036 percent of an extremely pungent volatile oil with an unpleasant odor.

EDITORIAL

DO THE OBESE REALLY EAT TOO MUCH?

In response to our recent Editorial, "Overeating," which appeared in the October 1952 issue, we were pleased to receive a reprint from Dr. M. Demole of Switzerland, entitled "Les obese mangent-ils vraiment trop?" from the Revue Medicale de la Suisse Romande LXXI, No. 10, Oct. 25, 1951. Demole asks the question whether obesity depends on superalimentation alone, or whether some basic metabolic fault is responsible. Already we are aware of the influence, in this connection, of the thyroid, the pituitary, the gonads and the mid-brain. It is easy enough to understand the obesity of the hypothyroid person (although, incidentally, the most markedly hypothyroid persons are not always fat), but it is more difficult to comprehend the obesity of the menopause. Constitutional obesity, though abetted by overeating, seems to depend upon the fact that lipid metabolism does not respond to normal regulations, although there is no proof at present that such is the case. Demole distinguishes between appetite and hunger, the former being possible only when the latter is appeased. According to the psychogenic theory, the constitutionally obese person is one who eats too much although he thinks he is eating normally. Demole also stresses the fact that many large eaters do not grow fat, also that some are known to become obese on 2,000 to 3,000 calories per day.

Demole wisely leaves it an open question—that is to say, the distinction between exogenous and endogenous obesity. It is certain, however, that, contrary to current accepted medical opinion (particularly in the U. S. A.), overeating is by no means the sole cause of adiposity. Until further, elusive factors in the production of endogenous obesity are known, our treatment of obesity will not likely prove too satisfactory.

BOOK REVIEWS

RETRO-PNEUMOPERITONEUM. L. de Gennes, J. P. May and J. Helie, Masson and Co., Paris, 1200 Francs.

This volume, well illustrated with x-ray films, deals adequately with the technique of retro-pneumoperitoneum—the insufflation of gas into the retroperitoneal spaces. 345 cases are studied, and the procedure is shown to be valuable in diagnosis, simple, and quite harmless. The method is chiefly of value in showing up the retroperitoneal organs.

A VITAMIN DIGEST. Guy W. Clark, Charles C. Thomas, Springfield, Ill. 1952, $6.50.

Clark, who is Technical Director of the Lederle Laboratories, has produced a very satisfying book because, in the case of each vitamin, he gives its source, its physiological effects, and goes into the clinical aspects of deficiency at the same time. The text is not overloaded with chemical formulae. For the physician desiring more direct and succinct information on human nutrition, especially from the vitamin aspect, the present volume is made to order, and is most highly recommended. The chapter on Thiamine is particularly excellent.

THE SPECIAL DIET COOK BOOK. Marvin Small. Greystone Press, New York, 1952. $2.95.

A 500 page volume at the extremely reasonable price of $2.95 is, in itself, unusual. The author is stated to be a leading dietetic expert who, through many contacts with doctors, dietitians and patients, became convinced of the great need for educational work in the field of special nutrition. There is an introduction by James R. Wilson, M.D., Secretary of the Council on Foods and Nutrition of the American Medical Association. The object of the book is not to encourage the lay reader to place himself on a special diet, but rather to assist the person for whom a special diet has been prescribed to prepare more attractive meals within the limits of the doctor's recommendation. Following are the types of diets described—low calorie, low sodium, high residue, bland, low fat and cholesterol, the diabetic diet and the high calorie diet. The bulk of the book is made up of recipes. It may be highly recommended to patients.

GENERAL ABSTRACTS OF CURRENT LITERATURE

HENRY, G. W.: *Emphysematous gastritis.* Am. J. Roentgen., Rad. Ther. and Nuclear Med., 68, 1, July 1952, 15-18.

Emphysematous gastritis is a phlegmonous gastritis caused by gas-forming organisms. Four cases have been found in the literature and a fifth case, that of an infant, is added. The x-ray appearance is characteristic and shows a mottled radiolucent zone, composed of gaseous blebs in the gastric wall, framing the stomach.

ADAMS, F. H., ANDERSON, R. C. AND RICHDORF, L. F.: *Four siblings with hepatic disease leading to cirrhosis.* Am. J. Dis. Child. 84, 2, Aug. 1952, 168-174.

This is a report of 4 sisters with hepatic disease leading to cirrhosis of the liver. All died under 2 months of age with symptoms of vomiting, jaundice, abdominal distension, and bleeding from the mucous membranes. No definite etiological factor could be identified. It would appear that an hereditary factor probably was operative.

WOLFSON, I. N.: *The use of para-aminosalicylic acid (PAS) in the treatment of intestinal tuberculosis.* Ann. Int. Med., 36, 6, June 1952, 1475-1483.

Three patients with intestinal tuberculosis were treated, with strikingly good results, with PAS. The sodium salt, 12 to 16 grams daily for 4 or 5 months was used. In two cases all clinical and x-ray evidence of the disease disappeared, while in the third, minimal abnormalities persisted. Cramps and diarrhea were the only toxic manifestations. PAS should be used in streptomycin-resistant patients, in those allergic to streptomycin, and in those where it will later be necessary to use streptomycin in combatting the pulmonary disease, which is always present.

RAVITCH, M.: *Consideration of errors in the diagnosis of intussusception.* Am. J. Dis. Child., 84, 1, July 1952, 17-26.

Errors in diagnosis of intussusception occurred in 19 of 79 cases treated at The John Hopkins Hospital between 1939 and 1951. In 18 of these cases, there was a consequent, significant delay in treatment. The child may appear relatively well in cases where a non-strangulating intussusception exists. Sometimes loose stools occur, which is very misleading. The failure to feel a mass does not by any means negate the diagnosis of intussusception. Early diagnosis requires a high measure of suspicion and ready resort to scout films and barium enemas. Where there is any doubt, laparotomy should be early undertaken.

DORSET, V. J. AND SPRIGGS, J. B.: *Diagnostic difficulties relating to amebiasis with 5 case reports.* Ann. Int. Med., 36, 6, June 1952, 1459-1466.

The manifestations of amebiasis are protean. Cases may clinically suggest appendicitis or perforated peptic ulcer, or carcinoma of the colon, Laennec's cirrhosis of the liver, and even pneumonia. Stool examinations, complement fixation tests, x-rays of the chest and G. I. tract are important aids in diagnosis in difficult cases.

TAKEDA, M.: *Studies on the motility of the gastro-intestinal tract by the electrical stimulation of the hypothalamus of rabbits.* II. Med. J. Osaka Univ., 4, Nos. 2-3, Feb. 1952, 149-175.

The author electrically stimulated first the ventromedial, then the lateral hypothalamic nucleus, with vagi intact, then with both vagi cut, and finally with right and with left vagus cut. He found that accelerated impulses from the lateral nucleus to the stomach and bowels were transmitted via both vagi; the right vagus gave a better response than the left; the rectum appeared to have no relation with the vagus nerve.

MASON, E. E.: *Gastrointestinal lesions occurring in uremia.* Ann. Int. Med., 37, 1, July 1952, 96-105.

Pathological anatomical alterations in the gastrointestinal tract are found in 60 percent of cases of uremia. Edema and hemorrhage into the mucosa and submucosa are the changes most frequently found. But in 19.6 percent of cases of uremia, ulcerative and pseudomembranous necrotic lesions were present. Renal diseases associated with extensive degenerative vascular changes in the body appeared to be more commonly accompanied by the gastro-intestinal lesions. Uremic ulcers and uremic pericarditis occur with the same frequency for the group as a whole. In 10 percent of 100 cases not having uremia, similar gastrointestinal lesions were found. The exact cause of the gastrointestinal manifestations is not as yet clear.

MODI, N. J.: *Some observations on cirrhosis of the liver.* J. Indian Med. Assn., XXI, 9, June 1952, 379-387.

37 patients in Bombay with hepatic cirrhosis and ascites were treated with a highly nutritious diet, supplemented with milk powder, brewer's yeast and casein hydrolysate. 15 patients were clinically cured, 10 showed fair improvement, 7 died, 3 showed no improvement, and 2 cases could not be followed. Increase in the serum albumin values were a good indicator of the patient's clinical improvement. The globulin fractions were of no value in this respect. In about half the cases, chronic alcoholism could be incriminated as causal, but malaria was an equally important cause. The salt-free diet seemed valuable, but the patients usually objected to it.

MORTON, T. C., STAMM, W. P. AND SEIDELIN, R.: *Indigenous amebiasis: A recent outbreak in England.* Brit. Med. J., July 19, 1952, 114-116.

An epidemic of acute gastro-enteritis and amebiasis at a Royal Air Force Station is described. In a population of 1,042 at risk, 141 suffered from acute gastroenteritis, 6 developed acute amebic dysentery and 11 had active amebiasis. Five of the six with acute amebic dysentery had been overseas. Twenty-six symptomless cyst-passers were found. Among 169 controls on the same camp, 6 symptomless cyst-passers were found but none with active amebiasis. Both the gastro-enteritis and the amebiasis are thought to have been water-borne, contamination of the station water supply having occurred from a broken sewer, so that gross fecal contamination of the water supply was responsible. The authors emphasize the insidious and protean nature of the disease and the possibilities of similar epidemics elsewhere.

DOUTHWAITE, A. H. AND SHAW, A. B.: *The control of gastric acidity.* Brit. M. J., July 26, 1952, 180-182.

Recognizing that Winkelstein's continuous milk and alkali drip is the most effective means of controlling gastric acidity, the authors sought to circumvent the practical difficulties of Winkelstein's method by having the patients with ulcer suck tablets made of milk solids and alkalis. Each tablet was about one inch in diameter and ⅓ inch thick. It is placed between the cheek and the teeth and sucked all the time, night and day.

Their results show remarkable and complete control of the gastric acidity. The reasons why swallowed doses of similar constitution do not control acidity is because such doses leave the stomach too soon. Each tablet contained solids from whole milk 40 gr., magnesium trisilicate 3.5 gr., magnesium oxide 2 gr., calcium carbonate 2 gr., magnesium carbonate 0.5 gr., plus oil of peppermint. The use of such tablets will hasten cure and prevent relapse of peptic ulcers.

HINKEL, C. L.: *Roentgenological examination and evaluation of the ileocecal valve.* Am. J. Roentgen., Rad. Ther. and Nuclear Med., 68, 2, August 1952, 171-182.

In every barium enema x-ray examination the ileocecal valve can almost always be identified and studied. Barium must enter the terminal ileum, and then graduated pressure applied to this area. The appearance of the filling defect at the valve orifice depends on the site of implantation of the ileum on the cecum, the size, shape and thickness of the valve lips and the degree of prolapse of ileal mucosa into the cecum. There is a wide range of normal variation in those aspects. Catharsis before the enema exaggerates the filling defect produced by ileal prolapse. Where the defects are of normal size, surgical exploration is not advisable. There is no reason to think that large or patulous valves should be resected. However, exploration is mandatory when large or peculiarly shaped defects cannot be differentiated with certainty from tumor of the valve lips.

SHIPPS, F. C. AND BRANNAN, D. D.: *Roentgenological findings in amyloidosis of the stomach.* Am. J. Roentgen., Rad. Ther. and Nuclear Med., 69, 2, Aug. 1952, 204-208.

Of the fifty cases of *primary* amyloidosis reported in the literature 13 were found to have x-ray or gross pathological abnormalities of the stomach. There may be gastric or duodenal ulceration, findings simulating cancer of the pylorus or antrum, or massive mucous membrane folds, with or without loss of peristalsis. Clues to the diagnosis are the symptoms referable to the organs involved in primary amyloidosis and the possible association of amyloidosis with myeloma or plasma cell leukemia. A case is reported in which the enlarged mucosal folds were obliterated by peristalsis.

BERGERET, A., ALBOT, GUY, BERTHET, G. AND HERMANT, J.: *Portal Hypertension of Biliary Origin. (External biliary fistula, splenomegalia and hematemesis due to portal hypertension following an injury to the choledoch: hepaticoduodenostomy, splenectomy and splenorenal venous anastomosis.)* Arch. mal. app. dig. T41 No. 9-10, Sept.-Oct., 1952, p. 865.

The authors insist on the importance of such a case which enables the biliary origin of certain portal hypertensions and certain splenomegalias to be proved. It would seem that the traumatic biliary fistula complicated by important sub-hepatic and pericholedocian inflammatory reactions is at the root of splenomegalia and hypertension discovered in the splenic vein by preoperatory manometry: hemorrhage did in fact appear six months after the injury to the choledoch and splenomegalia a year after this accident and the interference with the pericholedocian inflammation was probably not without effect on the portal vein.

LARSON, L. W. AND KLING, R. R.: *Pathology of gastritis.* Radiology 59, 3, 371. Sept. 1952.

Except for the difference in the size and number of the glands, the microscopic features of chronic gastritis are fundamentally the same whether the mucosal folds are larger or smaller than normal. The essential features are infiltration with inflammatory cells and alterations of the epithelial tissue. An exudative reaction may occur, however, which presents different histological findings from those described above. Here, polymorphonuclears appear in large numbers, particularly in the upper mucosa. There is a concomitant diminution in the mucous vacuolization which may extend well down into the glands. Russell's bodies are increased. This exudative reaction may be superimposed on any of the above described types of reaction. Numerous attempts have been made to correlate the gastroscopic, radiologic, and pathologic findings in gastritis. To date, these have not been entirely successful. There are seven illustrations to this article.

Franz J. Lust.

WEIGEN, J. F., PENDERGRASS, E. P., RAVDIN, I. S., AND MACHELLA, T. E.: *A roentgen study of the effect of total pancreatectomy on the stomach and small intestine of the dog.* Radiology 59, 92. July 1952.

Hyperglycemia in depancreatized dogs was found to be associated with delayed gastric emptying and with prolonged small-intestinal transit. Hyperglycemia in depancreatized dogs was associated with a normal and, at times, rapid gastric emptying and small-intestinal transit time. The absence of external secretion of the pancreas from the intestine did not appear to alter the tone or continuity of the small intestinal pattern or the tone of the colon. Loss of pancreatic function was not shown to alter gastro-intestinal motility while the blood sugar was low; its effects could not be evaluated while the blood sugar was elevated.

Franz J. Lust.

MARTIN, F. J. AND FRIEDELL, H. L.: *Partial obstruction of the small intestine—With special reference to the obstructing segment.* Radiology. 59, 1, 49. July 1952.

The roentgen diagnosis of partial obstruction of the small intestine has been discussed with special reference to changes which aid in localizing and studying the obstructing segment. The anatomical changes in the segment proximal to the lesion may indicate that a partial obstruction is present. One or more of the following abnormalities may be identified: a) gas within the lumen of the small intestine, b) an increase in the caliber of the small bowel as identified by either a barium mixture or intraluminal gas, c) abnormal mucosal pattern, d) delay in the transit time of the barium column, e) segmentation of the barium, f) abnormal position or mobility of the individual segments of the bowel, g) abnormal peristalsis. The obstructing lesion has been studied with reference to mucosal pattern, general contour and deformity, and behaviour during peristalsis. A number of cases of partial obstruction of the small intestine are reported.

Franz J. Lust.

DUBLIN, W. B.: *Problem of pathogenesis of chronic hypertrophic gastritis.* Radiology 59, 3, 377. Sept. 1952.

Chronic hypertrophic gastritis, duodenitis, and gastric and duodenal ulcer are regarded as manifestations of the same general process: vagal hyperfunction. Localization and type of injury and repair are affected by local factors, such as variation in vascular architecture and tissue resistance. Especially in the pyloric region, the hypertrophied muscularis may join contiguous submucosa in fibrosis; in this way, the firm ring of tissue is formed which is encountered in the condition referred to as antral gastritis. The fibrotic, thickened prepyloric muscle may lead toward the hypertrophied pyloric sphincter as a gradually thickened cuff, incorporating the sphincter, or in some cases ending just proximal to the sphincter, leaving a small intervening notch or segment of muscularis which is of relatively normal thickness. The proximal portion of the stomach may appear relatively normal; more often, there is at least some degree of chronic inflammation. The mucosal surface shows nodular irregularity. The intrinsic mucosal structure may be altered: except in cases of atrophy, the parietal cells appear reasonably numerous and capable of forming of acid. Lymphocytic infiltration may appear, especially in mucosa and submucosa. The latter may be edematous and fibrosed.

Franz J. Lust.

SEGAL, M., SEGAL, S., DEBRAY, C.: *A new technique of opacification of the small intestine by tubing in of the duodenum with obturation of pylorus.* Arch. mal. app. dig., T41, No. 9-10. 1952, p. 870.

The appliances amount to a "CAMUS" probe, bearing at about 8cm (3 inches) from the end a rubber olive, 12 mm in diameter somewhat bigger than the métallic olive at the end of the probe. The rubber olive when the probe is in place, obtures the upper-pylorus and prevents the flux down. Also a pressure injection apparatus for baryta; the latter is realized by means of a case-bottle with a double tubulure closely stopped; by injecting air through one of the tubulure, with a sound rubber pear, a strong pression is realized; through the other tubulure, reaching down to the bottom of the case-bottle, the baryta is blown by the air under pressure in the CAMUS-probe. The quantity of liquid to inject into the small intestine is from 500cc (cubic centimeters) to 1000cc.

The conveniences of this method are as such: 1) Simplicity of both method and material used; 2) Total avoidance of flow-back; 3) The rapidity of the transit runs on an average of 15 minutes, which allows for a full examination of the small intestine under radioscopic control; the peristaltic waves permitting, owing to the permanent oncoming of the baryta to study each segment several times.

Inconveniences: the inconveniences of the method are: 1) Necessity of tubing in the duodenum, but with a little training the putting in place is easily done; 2) A superposition of the ears, but owing to the non-absorption of water, the images are not compact and every ear may be dissociated with the feeler; 3) It is non-physiological method, but is not the barytal clyster by the back way a non-physiological method, which however proves greatly useful.

In short, this method will probably allow, by multiplying the examinations of the small-intestine, the showing up of jejuno-ileo organic lesions and perhaps individualize new syndromes.

AUGUSTE, C.: *Cure of a stricture of the esophagus of caustic origin after gastric resection.* Arch. mal. app. dig. T41 No. 9-10. Sept., 1952, p. 905.

The author reports the first known example of a stricture of the esophagus of caustic origin being cured after gastric resection.

The patient, who is now 55, in May 1942 swallowed a mouthful of washing soda in concentration. Three months later, there was almost complete dysphagia: radiological examination revealed a close stricture of the lower half of the esophagus, and esophagoscopy showed a scarred membranous funnel ending in a filiform opening, 31 cms from the dental arches. The dilatation enabled the patient to be fed fairly rapidly afterwards, but in December 1942 he underwent gastric resection as he was suffering from intolerable gastric burns apparently due to the gastric lesions caused by the caustic. The gastric secretion which had been hyper-hydrochloric became an-hydrochloric following the operation. Dilatation was resumed as soon as the patient recovered. The size of the aperture of the esophagus had already diminished but progress was rapidly made by bougienage, and two months later it was possible to introduce a number 40 French bougie. For 18 months the passage of the number 40 French bougie was continued, then all treatment was abandoned in 1944.

When seen again in March 1952, the patient was clinically cured. He could swallow solid foods and liquids more easily than in 1944, the diameter of the esophagus had not varied; radiological examination and esophagoscopy gave no indication of the existence of the lesions observed in 1942. The general condition was excellent.

The author submits that such an exceptional cure cannot be due solely to the effect of the dilatations and must be attributed to the additional action of the gastric resection. The most probable explanation is that the operation stopped gastro-esophageal regurgitation which was maintaining a latent peptic esophagitis, interfering secondarily to aggravate the sequelae of corrosive esophagitis.

The hypothesis is not unlikely in the case of this patient who bore lesions of the lower esophagus likely to obstruct evacuation of the stomach whose secretions had conserved a high acido-peptic strength until the operation.

The reported observation favors the opinion of Wangensteen who, in 1949, proposed treating strictures of the lower esophagus of caustic origin by gastric resection.

VACHON, A., BONNET, P. AND BERTHIER, J.: *Application of West's test in affections of the pancreas in adults.* Arch. mal. app. dig. T. 41, No. 1. Jan., 1952, p. 29.

West's test is based on the following principle: the absorption of a solution of gelatine causes a temporary increase in the amount of amino acids in the blood due to digestion of this protein by the trypsin of the pancreas; the curve of amino-acidity thus produced is able to give information on the functioning of the exocrine

pancreas since gastric pepsin does not produce amino-acids and erepsin from the intestine does not attack gelatine.

Applied by West and later by Walgreen in the study of fibro-cystic pancreatitis in children, this test may also be used with adults when an affection of the pancreas is suspected.

We have used West's test 52 times on 47 subjects of which 29 were check-patients free of any digestive trouble, and 18 suffering from or suspected to be suffering from a disease of the pancreas: 4 cancers, 5 certain cases of pancreatitis, 9 probable or possible cases of pancreatitis.

1. THE AMINO-ACIDITY CURVE OF THE CHECK-PATIENTS

The basic amino-acidity figure varies from 4 to 8 mgs per 100 and the increase, starting from this initial figure, is 1.5 mg to 2 mgs in ½ hour, 3 to 4 mgs in 1 hour, 4 to 6 mgs (and sometimes more) in 2 to 3 hours; the curve falls afterwards returning to normal after 4 hours or a little later.

A curve is manifestly abnormal when it remains lower than 2 mgs during the entire period of the test, but when at the end of an hour the increase in the amino-acid content is not higher than 2.5 mgs, the curve may likewise be considered pathological, even if there is a subsidiary rise in the curve.

2. THE AMINO ACIDITY IN CANCER OF THE PANCREAS

Out of 4 cases (two non-icteric cancers of the body and two icteric cancers of the head) the test is positive 3 times and negative once. In two cases, the curve obtained is comparable to the one obtained by West in fibro-cystic pancreatitis in children.

3. THE AMINO ACIDITY CURVE IN CHRONIC PANCREATITIS IN ADULTS

Out of 5 certain cases of pancreatitis, whether or not in association with biliary lithiasis, after an operatory check West's test proved positive in 4 cases: a flat curve below 1.5 in 1 case (diffuse pancreatitis); a curve rising no higher than 2.5 by the end of an hour in 3 cases.

Out of 9 probable cases of pancreatitis, not verified by a surgical operation: 5 positive reactions to West's test.

CONCLUSIONS

The amino-acidity curve induced by the ingestion of gelatine may be applied in pancreatic disorders in adults. It may, if positive, offer a useful complement to the clinical diagnosis and be compared with other laboratory tests. Certain sources of error must be eliminated: in particular, delay in the absorption due to gastric or intestinal stenosis. The test may prove faulty if the excretory canal is not compressed and if lesions allow a sufficient quantity of parenchyma to be secreted.

CARLISLE, J. C. AND JUDD, E. S., JR.: *Regional enteritis involving the duodenum: report of case.* Proc. Staff Meet., Mayo Clin., Dec. 31, 1952, 27, 569-574.

Previously only 9 cases of proved regional enteritis involving the duodenum have been reported. Now the authors report one more case, which presented tremendous difficulty in diagnosis, even at laparotomy. Later it was found that the same process was at work in the small bowel.

SALTZSTEIN, H. C., MAHLIN, M. S. AND SCHEINBERG, S. R.: *Bleeding peptic ulcer.* Harper Hosp. Bull., 10, 6, Nov.-Dec. 1952, 160-167.

Possibly the outstanding point in this article is the finding of the authors, that many persons with bleeding ulcers will eventually stop bleeding if transfusions of blood are continued long enough, in fact longer than is usually practiced. Operation is, of course, done when necessary.

ANDERSON, W. L.: *Primary carcinoma of the duodenum.* Harper Hosp. Bull., 10, 6, Nov.-Dec. 1952, 178-183.

Primary cancer of the duodenum is a rare condition and presents extreme difficulty in diagnosis. A case is described in which distant metastases caused the first symptoms, the primary lesion being recognized later when vomiting began.

SAINT, E. G.: *Infectious hepatitis in older age groups.* Med. J. Australia, Nov. 1, 1952, 613-619.

Twenty cases—10 men and 10 women—aged over forty years, suffering from infectious hepatitis, are reported. The manifestations of infection were more severe than in younger patients. In 4 cases (with 2 deaths) the infection was severe and fulminant, and in 4 cases (with one death) there were several relapses and the development of advanced cirrhosis. Severe right upper abdominal pain mimicked that of gallstones or pancreatic cancer. The cephalin flocculation and serum alkaline phosphatase tests supply the most valuable information. Aspiration biopsy is of limited diagnostic value unless done shortly after the onset of jaundice.

BROWN, G. W.: *Anaerobic paracolon bacilli associated with gastroenteritis in children.* Med. J. Australia, Nov. 8, 1952, 658-664.

A group of paracolon bacilli with distinctive characteristics were isolated in all of 13 cases of gastroenteritis in children at the Adelaide Children's Hospital. Specific agglutinins of this group were also found in the sera of the 13 cases. These organisms and these agglutinins were absent from the feces and sera of normal children and from children with known Salmonella and bacillary dysentery infections. It would appear that this "A.C.H." group can cause mild gastroenteritis.

NASIO, J.: *Medical Treatment for Chronic Ulcerative Colitis.* American Journal of Proctology 3:45-58, March 1952.

On the basis of 10 years' experience in the medical treatment of C. U. C., the author studies in a most complete manner, the rational treatment of this disease—by which means a good percentage of perfectly controlled medical cures have been obtained after three years. Seventy-three cases of patients between the ages of 30 to 40 years are studied, in the proportion of 39.8%; from 20 to 30 years of age in the proportion of 26%; from 10 to 20 in 13.7%; from 50 to 60 in 2.7% and 1.4% in patients of less than 10 years of age. Feminine sex: 50.7%, masculine: 40.3%. The

evolution time of these cases has been from 3 to 10 years in 70% ; from 1 to 3 years in 25% and only 5% of these more than 10 years. The treatments employed have been in accordance with original experience of the author, such as the hormono-vitaminic treatment; in 100% of the cases, the "drop by drop" treatment of colitis, by means of hydroxide of colloidal aluminum in 43.8% ; penicillin in 32% ; sulphamides in 26% ; streptomycin in 20.5% ; tyrothricin in 13.7% ; and aureomycin in 4.1% . All these treatments were applied, many of them in one same case hormono-vitaminic, or in other words, the continuation of hexestrol, calcipherol and ascorbic acid in high doses all by parenteral way were employed in all cases.

The results, adequately controlled, from a radiologic, clinical and endoscopical point of view, have exhibited the following proportions: Therapeutical prognostications: Excellent, 30.1% ; good, 30.1% ; fair 20.5% ; bad-interventions, 12.3% ; interruption of controls, 6.8% . The relation between the evolution of the disease and its therapeutical prognostication or the evolution under the different treatments have been as follows: 59% of excellent or good therapeutical evolution in patients of less than three years evolution. On the other hand a bad or fair evolution was produced in 61% of patients with less than three years evolution and in 39% of patients of more than three years evolution.

The new medical treatments of C. U. C., particularly the hormono-vitaminic and "drop by drop," which the author advises, have been applied with excellent benefits in Italy, Uruguay, Chile, Mexico, Brazil, Spain and the United States of America. Their application and control corresponds to the realization of Gastroenterologists.

BROMBART, M., LAURENT, Y., GODART, J.: *Benign ulcer of the esophagus associated with a duodenal ulcer. Its relations with esophageal dyskinesia.* Arch. mal. app. dig. No. 5. 1952.

The authors report on a case of peptic ulcer of the esophagus associated with duodenal ulcer and esophageal dyskinesia in a 39 year old man.

The roentgen diagnosis was confirmed by clinical findings, endoscopy, operation and later evolution.

The noted dyskinesia was made manifest by secondary contractions which originated in the median ⅓ of the esophagus, spreading either downwards or in cephalic direction (antiperistaltism).

The peptic ulcer of the juxta-diaphragmatic segment of the esophagus showed typical roentgenological appearance. The duodenal ulcer was of the scarred type.

The general condition of the patient was improved by gastrectomy, which had to be completed by esophageal dilatations producing the disappearance of the ulcer niche and stenosis.

Esophageal dynamic disorders were still observed one and one half years after the treatment was suspended.

The authors stress the extreme rarity of the esophageal peptic ulcer not associated with brachyesophagus and roentgenologically diagnosed. This rarity becomes particularly obvious when compared with the extreme frequency of duodenal ulcer.

The elements of the roentgen diagnosis of esophageal ulcer are exposed, its etiology and pathogeny discussed. Cardia spasms, which had been observed in their patient before appearance of the duodenal ulcer and the peptic ulcer of the esophagus, are supposed to have favoured the formation of the latter.

The authors think that the esophageal dyskinesia manifested by secondary contractions persisting still one and a half years after the clinical and radiological healing of the narrowing of the esophagus and the ulcer are in relation with irreversible changes of the intraparietal nervous components, owing to the chronic inflammatory processes in the neighborhood of the ulcer.

DOCTORS CATTAN, CARASSO, CHAMPEAU AND BLOCH-LAROQUE.: *Hemorrhagic recto-colitis.* Arch. mal. app. dig. No. 5. 1952.

In connection with the observation of a serious hemorrhagic colitis, first treated medically, later surgically, and resulting in recovery, the authors make a particular study of a new method of restoring continuity after complete colectomy and amputation of the ampulla of the rectum.

This method of restoration is only valid where both the colon and the rectum have to be completely removed but where the mucous membrane of the anal canal and the sphincter can be retained.

There are two important points:

1.) The first stage of the operation consists of a colostomy of the right iliac fossa retained by a stick.

The authors consider that this method is superior to ileostomy: there is no operatory mortality, it is easy to perform, there are no complications such as volvulus of the small intestine.

Colostomy carries off matter just as efficiently and with less trouble than ileostomy. Subsequent secondary exeresis difficulties are no greater.

2.) The exeresis operation.

It has the advantage of being completed in one operation. The restoration of continuity will be achieved systematically as the new technique makes for good continence. It is for this reason that it is superior to definitive ileostomy and the termino-terminal suture of the ileum at the anal canal.

This technique consists of a latero-terminal anastomosis at the anal canal about 70 cms above the ileal section. This suture is performed by way of the endo-anal tract with evagination of the mucous membrane of the anal canal. The suture is therefore made on the outside and later put back into place.

This distal section of the ileum is grafted in termino-lateral anastomosis on to the small intestine above the ileo-anal anastomosis.

In this way, a circuit is formed which helps continence in the following manner:

When the fecal bolus reaches the sphincter, anastomosized laterally, the latter is warned in time and has sufficient strength to prevent any escape. The contents of the intestine pass into the ileal loop and then return to their original tract. Such a circuit may be repeated for a long time. In this way collisation may take place whilst the perineum is protected.

Initial results obtained by these authors are excellent.

MONGES, H. AND A., GUIGOU, CH. AND BOUILLIN, PH.: *Investigation of hypoglycemia in gastrectomized patients.* Arch. mal. app. dig. No. 5. 1952.

The authors have made a study of the effect of the ingestion of fats on glycemia in gastrectomized patients (subtotal gastrectomy for ulcer); they give the results obtained with crude olive oil after a dose of 40 to 50 cc. At the same time they have investigated the effects on the glycemia of non-gastrectomized patients of the ingestion, on the one hand, and of the instillation, on the other hand, of the same quantity of oil in the duodenum. The glycemic doses were administered before the doses of oil and later every quarter of an hour during the first hour and every half-hour during the following two hours.

The following facts emerge from this research:

1. With 2/3 of the gastrectomized patients (11 times out of 17) the ingestion of oil brings about definite hypoglycemia (30 to 45%) whose peak occurs after ½ to 1 hour after the commencement of the test.

2. With normal patients, the ingestion of oil does not noticeably modify the rate of blood sugar; on the contrary, direct administration into the duodenum of the fat by tubing, brings about almost consistently (11 times out of 13) a lowering of glycemia fairly similar to that obtained with gastrectomized patients after ingestion.

The recorded lowering of glycemia in gastrectomized patients after ingestion of oil, and with intraduodenal instillation of this substance in normal subjects is attributed by these authors to the massive liberation of the duodenojejunal hypoglycemic hormone (La Barre's incretine). The slow gastric evacuation of the oil in normal subjects after oral administration explains the absence of notable variations in glycemia.

The authors show the importance of their investigation on the diet to be prescribed for gastrectomized patients.

FROEHLICH, A. L. AND BUYSSENS, N.: *Contribution to the study of steatorrheas.* (*Contribution a l'etude des steatorrhees*). Acta Gastro-Enter. Belgica 15, 6, 487. June 1952.

The clinical features of 12 cases of idiopathic steatorrhea and of 3 cases of lambliasis and 2 cases of anatomical lesions of the small intestines have been described. The diagnosis of steatorrhea is admitted when the percentage of fat in dry feces exceeds 20%; about 70% of the total fat content is hydrolyzed. The use of an emulsifying agent in three cases had diminished on the average by 16%, the mean value of fat in dry faeces, and increased the amount of hydrolysis by 19%. In half the cases of idiopathic steatorrhea, free hydrochloric acid has been found after histamine stimulation. The amount of choline in the bile from the bile duct is about 110 mg%, that of bile salts is 220 mg%. In three cases of steatorrhea, no choline nor bile salts could be detected in bile from the duodenum. Calcaemia is usually low, between 9.5 and 5.4 mg%; phosphoremia is less frequently reduced to between 1.25 and 2.4 mg%. Proteinemia is regularly low. This must be ascribed to a fall of serum albumin. Lipaemia is also reduced. The percentage of hyperglycaemia after feeding of glucose does not exceed 10%. A fall in blood sugar generally occurs in due course.

After feeding of a fat meal, hyperlipaemia does not occur. This may be ascribed to a lack of increase of neutral fat. Cholesterolaemia and phosphatidaemia increase as usual. The radiological examination of the small bowel discloses either hypotony and hypomotility or increased peristalsis and hypertony. Neither of these aspects can be connected with the severity of the disease. A necropsy has been performed in four cases. The findings disclose a chronic infiltration of the mucosa with mononuclear cells and some fibrosis and also regressive changes in the small intestine.

Franz J. Lust.

JENKINSON, E. L., PFISTERER, W. H., NORMAN, R. C. AND LATTEIER, K. K.: *Perigastric adhesions and bands involving the pyloric antrum.* Am. J. Roent., Rad. Th. 67, 2, 210. Feb. 1952.

Lesions of the pyloric antrum are of equal interest to the diagnostician and the surgeon. Close cooperation is essential to identify such lesions early. Should the conclusion leave any doubt as to the presence of a malignant or potentially malignant lesion, surgery is advisable. Prepyloric defects that persist after administration of antispasmodic and medical management should be subjected to surgery. To find no lesion at operation in the presence of persistent roentgenological defect is definitely better than at a later date to find an inoperable malignancy. Persistent roentgenological defects do occur in the absence of surgical proof. In the light of the authors' present knowledge, it is often impossible to differentiate, clinically or roentgenologically, pyloric defects. Unfortunately, gastroscopic examination does not clarify the diagnosis. Several roentgenograms and drawings of the operative findings in perigastric adhesions illustrate the article.

Franz J. Lust.

BACKGROUND MATERIAL: THE AMERICAN FOUNDATION OF TROPICAL MEDICINE

In early January, 1953, after long and careful consideration of candidates for the post, the American Foundation for Tropical Medicine appointed a research director for its Liberian Institute in West Africa. With this event the Liberian Institute, conceived in 1946, began to exist in fact; and its parent body, the American Foundation for Tropical Medicine, started an important expansion of the program it created twelve years ago with these objectives:

To develop new knowledge that will contribute to the treatment, control, or suppression of tropical diseases, and

To educate young physicians, sanitation officers, and scientific investigators in the problems and practice of tropical medicine.

Diseases for which no known cure exists continue to shorten the lives and sap vital energies of millions of people living in the tropical areas of the world. In stifling productivity, they continue to retard social and economic development of tropical countries, and to keep vast populations in ignorance and misery.

Today, the threat of tropical diseases, and their consequences, extends far beyond the tropics. Increasing world trade and travel have shortened the distance that once separated peoples, and countries, and have brought the implications of tropical disease to our own doorstep. Research in tropical medicine should be of more than academic—or altruistic—interest to the people in the United States.

When large-scale military operations in the Pacific were entered upon by our country in World War II a serious shortage of medical men trained in tropical medicine was revealed. As a result military operations were seriously handicapped until special training could be set up to equip doctors and public health officers with the scientific knowledge needed to control health and disease conditions where troops were located. The American Foundation for Tropical Medicine provided funds that assisted several medical schools to give instruction in tropical medicine to students preparatory to service in tropical war zones. Now the Foundation will be able to provide additional and broader education in tropical medicine and disease at the Liberian Institute in Harbel, Liberia.

Today, the scarcity of men trained in tropical medicine still exists in human medicine, public health and sanitation and research. While the potential consequences of this lack are not as far-reaching as was the scarcity revealed at the start of World War II, its implications are still serious.

Military personnel is still required to maintain installations in tropical regions. Men who understand tropical disease are still required for the health protection to military forces. But even if there were no military demands, there would still be a large civilian need of doctors and public health officers with tropical experience, owing to the increase in Americans who represent both Government and business and industry in tropical countries.

The American Foundation is now in a position, for the first time, through the Liberian Institute, to provide unusual and greatly needed opportunities for field training in tropical medicine to students, doctors, public health and sanitation officers and scientific investigators. These facilities will be of particular value to American students preparing for a career in the field of tropical medicine.

Until now, American medicine has been seriously handicapped by the lack of facilities of this kind. The same handicap has existed for the field testing of drugs and insecticides that are now being developed to combat or control tropical infections. The Liberian Institute is offering its facilities to drug and pharmaceutical companies to meet this lack.

The Foundation's chief research activities at present are centered in its Liberian Institute where a program of research will be undertaken into three major problems which contribute to the backwardness of tropical countries: the communicable diseases of man; the inadequate animal husbandry responsible for chronic protein deficiency, and the establishment of an agricultural economy adequate to the needs of men and animals. Studies of the diseases of man will be the first research undertaking.

It is known that malaria, amebiasis, filariasis, sleeping-sickness, yaws and schistosomiasis are widely distributed over Liberia. However, no comprehensive survey has been made of the incidence and distribution of all of these.

Infection rates of malaria are known for some of the provinces, for example, but little is known of that of filariasis. The surveys of schistosomiasis so far made have been confined to provinces bordering French Guinea and the Ivory Coast. A survey of this disease is urgent since it is believed probable that it is a major cause of the chronic illness and disability among the population. Also, little is known of the distribution of trypanosomiasis (sleeping-sickness). A small amount of work has been carried out on the tsetse fly in Liberia, but most of the studies have been confined to the western province, and practically nothing is known of the vectors in other parts of the country.

The American Foundation for Tropical Medicine is prepared and equipped to undertake in Liberia a survey of the endemicity of malaria, schistosomiasis, intestinal parasites, trypanosomiasis, filariasis and leprosy. The hope is to study the distribution of these diseases in six sample areas of the country: in the northern, northwestern and eastern portions, in two sections of the coastal area, and in the capital city of Monrovia. Six months to a year would be required for a survey of the kind described if carried out by a team of eight to ten scientists and technicians.

The Liberian Institute, established in 1946 to provide a specialized laboratory center in the tropics in which scientists can work together in a common drive to conquer tropical diseases, is located on 100 acres of land which was donated by the Liberian Government.

The Institute is situated near Monrovia, the capital city, and lies within a section equipped with electricity, pure water, roads and road maintenance. In addition to its mechanically complete facilities, the Institute can offer scientists and investigators opportunities for clinical study in a nearby modern hospital.

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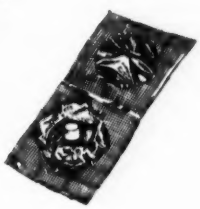

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*Beckman, H.: Pharmacology in Clinical Practice, Philadelphia, W. B. Saunders Company, 1952, p. 361.

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possible construction of a modern two-story, two-wing laboratory building and three two-bedroom residential houses. Additional residential buildings will be constructed on the property as soon as possible with funds already given to the Foundation by Mr. Firestone for this purpose.

Liberia, located on the West Coast of Africa, offers an unusual vantage point for a research center in tropical diseases, since a wide variety of tropical diseases have long been endemic there. Further, Liberia offers an auspicious political climate for the location of a scientific institute as a republic free of the international politics and entanglements of Europe and Africa.

There is inevitably a similarity in

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the conditions under which tropical diseases flourish: the extreme poverty, the economic and social backwardness, and the inadequate nutrition. This being so, the study of any tropical disease in its natural environment in any one place will be of value in the treatment, control and/or suppression of the disease wherever it may exist.

Facilities of the Liberian Institute will be made available to visiting scientists and graduate medical students, without restriction as to race, to carry on independent research in health and nutrition in the tropics. Any findings of the Institute will be available to any individual scientist or group of scientists working on problems of tropical medicine and the Institute will, in time, become a clearinghouse of information on tropical disease.

Scientific activities in the Institute will be under the supervision of a Scientific Advisory Committee of the Foundation, composed of scientists drawn from the faculties of 22 American colleges and universities, and medical representatives of industrial organizations. Approval by the Committee will be required of any project carried out at the Institute by any individual or group not directly affiliated with the Institute.

In January, 1953, the American Foundation for Tropical Medicine appointed Dr. Max J. Miller, Assoc. Professor in the Institute of Parasitology of Macdonald College, McGill University, as the Institute's first research director. With the appointment of Dr. Miller the Institute thus arrives at a position to start its aggressive campaign which will, in time, undertake research in two additional fields whose problems are related to those of tropical disease: in animal husbandry, and in agriculture.

The inability of domestic animals in tropical countries to withstand tropical diseases has heretofore prevented the successful raising of livestock in those countries. Development of animal husbandry in these lands is essential to any solution of the chronic protein deficiency which has been the chief cause of widespread malnutrition and susceptibility to disease of the people.

An attack upon the nutrition problem in the tropics is closely related to the problem of disease of man and study of disease of animals becomes essential to effective research program in tropical disease. The Foundation, in conceiving the Institute, determined to make animal husbandry and veterinary medicine an integral part of its research program.

The Foundation will endeavor to introduce and breed a strain of domestic cattle capable of enduring the heat of the tropics, able to withstand infection by such tropical diseases as ngaga and tryptosomiasis, and to survive on the existing agriculture of the country.

The production of balanced food crops for both man and animals is essential to any lasting victory over diseases attacking animals and humans in the tropics. The three problems of disease of man, disease of animals, and the development of an adequate agriculture must be studied together.

NEW MEDICINALS REVIEWED BY 150 REPRESENTATIVES OF PARKE, DAVIS & CO. AT SAN FRANCISCO MEETING MARCH 19-21

San Francisco — Approximately 150 representatives of Parke, Davis & Company who contact physicians and pharmacists in 13 Western states reviewed medicinals at a meeting in the Palace Hotel here March 19-21.

Several top executives from the home offices of the pharmaceutical firm, headed by Harry J. Loynd, president, participated in the three-day sessions.

Others included Graydon L. Walker, vice-president and director of U. S. and Canadian sales and promotion; Carl Johnson, U. S. and Canadian sales manager; Frank Nelden, manager of medical sales education; Dr. J. E. Gajewski of the Department of Clinical Investigation; H. B. Rames, chain store sales manager; and M. W. Dicks, assistant manager of hospital and biological sales.

Besides new medicinals, the representatives discussed pharmaceutical market conditions and 1953 sales plans. Co-chairmen were these four branch managers: G. C. Tasker of San Francisco, W. J. Roberts of Los Angeles, H. R. Tennant of Seattle and V. F. Jochems of Denver.

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CIBA

Dr. Frederick R. Yonkman, vice president in charge of research for Ciba Pharmaceutical Products, Inc., Summit, N. J., has been elected to serve as a Trustee of the Columbia University College of Pharmacy, it has been announced by M. A. Dittmar, secretary of the College. Dr. Yonkman's three-year tour of duty will begin on July 1, the start of the new academic year.

Dr. Yonkman, who is on the teaching staff of the College of Physicians and Surgeons of Columbia, is a director of the American Pharmaceutical Manufacturers Association, as well as several other medical and scientific societies. He is recognized as an outstanding authority on high blood pressure and its relationship to disorders of the sympathetic nervous system. He was appointed vice president in charge of research for Ciba in December, 1952.

CIBA

T. F. Davies Haines, president of Ciba Pharmaceutical Products, Inc., Summit, New Jersey, announced the appointment of James R. Beattie as director of public relations at Ciba's Summit operations.

Mr. Beattie first joined the Ciba staff in 1946 at Summit, being assigned to the Medical Service Division. In 1952 he was transferred to the Advertising Division.

Mr. Beattie, born in Philadelphia in 1922, graduated from Phillips Exeter Academy and Princeton University. He attended the University of Pennsylvania School of Medicine for three years.

FURADANTIN IN INFECTIONS OF THE GENITOURINARY TRACT

Furadantin, a new nitrofuran, was administered systemically by the oral route to fifty ambulatory patients having acute or chronic genitourinary tract infections. The results of this study indicate it to be a safe and effective agent having a broad antibacterial spectrum. No case of sensitization has occurred.

In a few instances, *in vitro* tests indicated apparent resistance of the bacteria, but negative cultures and absence of symptoms following treatment affirmed the clinical effectiveness of Furadantin. Only four of fifty patients failed to show improvement.

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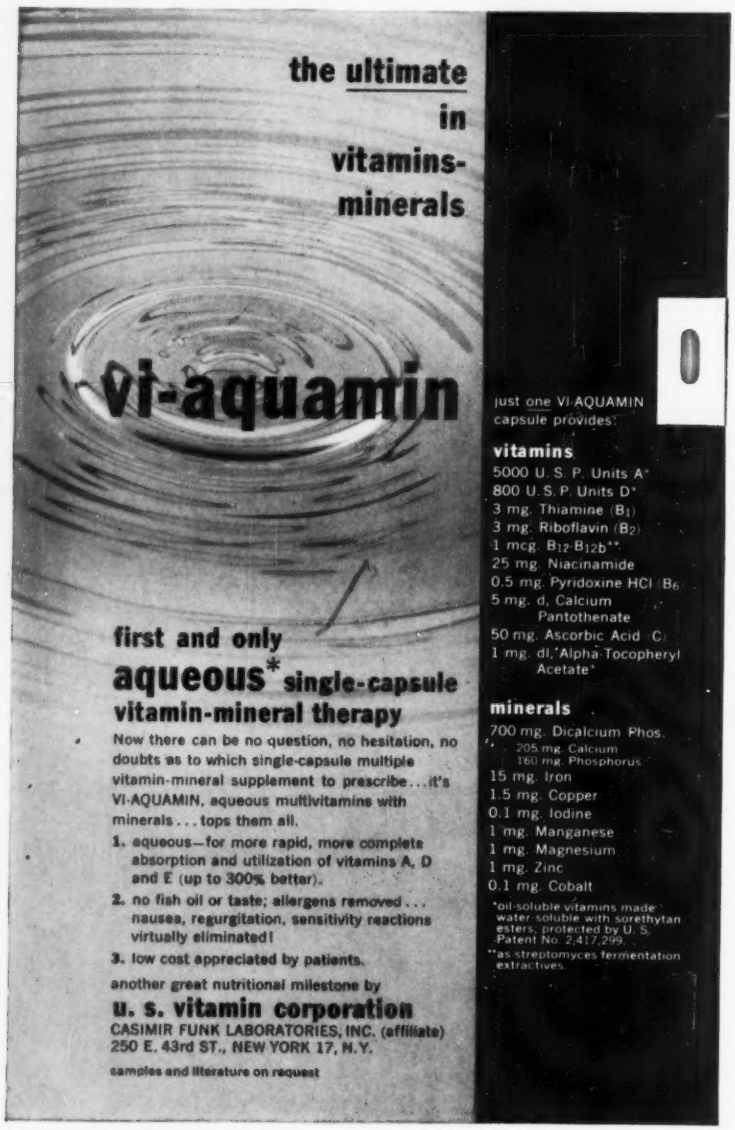
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Fig. 1: "Roentgen examination . . . revealed the ulcer to be very much in evidence."

Fig. 2: In ten weeks "the ulcer niche was no longer in evidence roentgenologically or gastroscopically."

Clinical Evaluation of Pro-Banthine*

CASE REPORT

"M. D., female, aged 48, had a posterior gastrojejunostomy 14 years ago for duodenal ulcer. The patient was fairly well until nine months ago when severe, intractable pains occurred. She was hospitalized and a subtotal gastrectomy was done.

"She remained well for only a few months and was referred to us because of recurrence of very severe pain and marked weight loss. Roentgen study revealed a fairly large ulcer niche on the gastric side of the anastomosis.

"The patient had been on various types of antacids and sedatives without relief from pain. She was given 60 mg. of Pro-Banthine q.i.d. and within 72 hours was able to sleep through the night for the first time in weeks.

"At the end of two weeks of such treatment the patient had absolutely no pain and felt that she had been 'cured.' Roentgen examination at this time revealed the ulcer to be very much in evidence (*Fig. 1*). Much persuasion was necessary to make the patient realize the importance of maintaining her diet and therapy.

"Ten weeks of controlled regulation was necessary before we were satisfied that the ulcer niche was no longer in evidence roentgenologically or gastroscopically (*Fig. 2*).

"She has been maintained on 30 mg. [q. i. d.] of Pro-Banthine for almost five months with no recurrence of symptoms."

Schwartz, I. R.; Lehman, E.; Ostrov, R., and Seibel, J. M.: A Clinical Evaluation of a New Anticholinergic Drug, Pro-Banthine, to be published.

Pro-Banthine (*brand of propantheline bromide*), the new, improved anticholinergic agent, is more potent and, consequently, a smaller dosage is required and side effects are greatly reduced or absent.

Peptic ulcer, gastritis, intestinal hypermotility, pancreatitis, genitourinary spasm and hyperhidrosis respond effectively to Pro-Banthine, orally, combined with dietary regulation and mental relaxation.

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